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CARCINOMA OF COLON AND RECTUM*

Observations on Massachusetts General Hospital Cases, 1937-1948

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BOSTON

TWO basically conflicting trends in the treatment of cancer of the colon and rectum are evident today. One school of surgeons, believing that present results are excellent, attempts to limit the number of radical operations and advocates the preservation of sphincters. The other school, apparently feeling that today's results are poor, advocates more extensive surgery than has been done in the past. Both groups have produced apparently logical support in the surgical literature, on both pathological and statistical grounds.

The student who attempts to correlate the various statements that have been made in recent publications will therefore recognize many unsolved surgical problems and in addition will be perplexed when he tries to compare results in different localities. In an attempt to clarify the situation, we have made a comprehensive study of all cases of cancer of the colon and rectum treated in the Massachusetts General Hospital, on both wards and private services, between January 1, 1937, and January 1, 1949.§

A spirit of optimism is begotten by the surgeon who analyzes his figures, discarding cases in which no operation was performed as well as palliative resections, deaths from operations, later deaths from extraneous causes and those patients who have not been followed. He, obviously, ends with a comparatively high percentage of "cancer cures." Thus, according to certain selective methods of statistical analysis, "five-year cures" are currently reported in as much as 68.7 per cent of cases[1] — and even in 93.3 per cent if only the most favorable cases are considered.[2] Such a system is manifestly unfair to any student of public health or to anyone who wishes to consider the entire problem of cancer of the colon and rectum rather than a highly selected group of cases, since in any complete survey unfavorable cases cannot be discarded.

By contrast, Ottenheimer,[3] in his analysis of 1610 cases of cancer of the rectum admitted to Connecticut Hospitals in 1935–1945, found that five-year survivals were shown in 7.9 per cent of all cases, although his more recent figures show significant improvement.[4] Similar poor figures for gross five-year survival of all cases seen range from 5.6 per cent to 11.3 per cent, as reported from smaller hospitals.[5-8] Gross five-year survivals in all cases seen in the larger clinics are more difficult to compute from published figures but are apparently of the order of 20–30 per cent. In the present series, this figure is 26 per cent.

This extreme disparity of results suggests that more is involved than the quality of surgery available and that the selection of cases included in any reported series is effectively hiding the actual facts. The first problem, then, is to select the best method of computing figures. Several methods are available; all have disadvantages. The two best methods are:

(1) Survival rates are calculated on the basis of all cases that appear in the given clinic or geographical area. Considering the entire problem of cancer this is the best method of all, but it has certain inherent difficulties. Thus, hospitals that draw their patients from a wide area and from a distance are likely to attract a more favorable group for cure. A moribund patient might well be carted around the corner to die promptly in a city hospital but would not be put in an ambulance for a trip of several hundred miles. Furthermore, clinics that deal with private patients secure a more favorable group for cure than the charity hospital. This fact was brought out years ago by Simmons and Taylor[9] in their studies on breast cancer and has been recently emphasized by Garlock and Klein[10] with reference to the colon. The same impression is gained from a study of these particular cases. Finally, the number of five-year survivals may be

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so small that the results from variations of surgical therapy are not apparent in the statistical analysis.

(2) Survival rates are calculated on a base of the patients on whom resections for cure were performed (that is, all cancer removed, so far as the surgeon could tell), excluding operative deaths only. Although this is apparently a valid basis for comparison, the surgeon who performs extensive operations on old persons and on those suffering from other debilitating diseases will have a lower percentage of patients surviving five years, even though he may make more patients comfortable for longer periods of time.

We believe that computations according to both methods should be included in all reports of cancer survival. The main objection to many discussions in the literature is that the author fails to specify the method used to calculate his results. His figure is then quoted by other authors without qualification, and it becomes almost impossible to compare results from different hospitals.

We believe that it is inaccurate to exclude deaths from other causes in any follow-up study unless autopsies have been done routinely, for otherwise the presence or absence of cancer at death cannot be determined accurately. We have counted all the patients who have been lost to follow-up as dead of cancer in the last year that they were seen. This practice was established by Greenough and Simmons in this hospital and has been found to stimulate an accurate and intensive follow-up. We have used the term "five-year survival rate" rather than "cure." It is well known that some patients who are living five years from the date of operation with no evidence of disease will later die of recurrent cancer of the bowel. There is no year in which one can be certain that a cure has been achieved. Therefore, to use such a term is misleading.

Of the cases reported in this paper (Table 1) 1088 were seen in the period from January 1, 1937, to January 1, 1944, and the five-year survival rate was determined for this group. All patients who entered the hospital are included. All but 20 were followed until recurrent cancer was diagnosed, until death supervened or until at least five years had elapsed after the date of operation. The 20 cases lost to follow-up from the entire series are counted as dead of cancer.

In the course of the study a number of important features were encountered that entail further comment and will be discussed in more detail.

Delay to Treatment

The delay between onset of symptoms and admission to the hospital averaged seven months during the entire period of the study (Fig. 1). There has been no significant change through the years, nor has there been any increase in the percentage of patients who entered the hospital within a month of onset of symptoms. The delay to treatment after onset of symptoms averaged seven months for the right colon, 6.5 for the transverse, 6 for the left, 7 for the sigmoid and 7.5 for the rectum.

It is impossible to determine the responsibility for this delay by means of the records. It probably must be assumed jointly and nearly equally by the patient and the physician. However, even the pa-

TABLE 1. *Distribution of Cases of Carcinoma of Colon and Rectum, Massachusetts General Hospital, 1937–1948.*

	1937–1943				1944–1948			
	No Operation	Minimal Palliative Operations	Palliative Resection	Resection for Cure	No Operation	Minimal Palliative Operations	Palliative Resection	Resection for Cure
Colon	26	123	46	291	20	62	47	277
Rectum	35	116	49	386	19	62	48	333
Anus	1	3	0	12	0	0	0	5
Totals	62	242	95	689	39	124	95	615

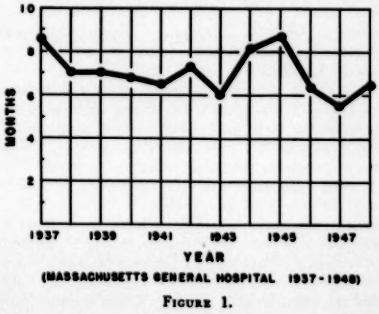
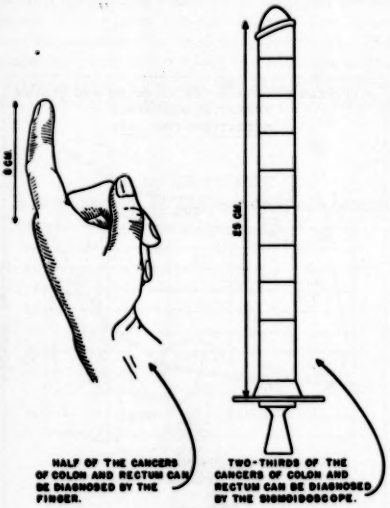


FIGURE 1.

tient who reports soon after noting his initial symptom is still in a far from enviable position with respect to cure. Thus, in the 115 patients who were admitted to the hospital less than a month after onset during the years 1937–1944, only 24, or 21 per cent, were living five years later. Interestingly enough, the survival rate appears somewhat higher in patients who entered with a dramatic onset of symptoms, such as acute obstruction; 33 entered within a week of noting the first symptom, and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HALF OF THE CANCERS OF COLON AND RECTUM CAN BE DIAGNOSED BY THE FINGER.
TWO-THIRDS OF THE CANCERS OF COLON AND RECTUM CAN BE DIAGNOSED BY THE SIGMOIDOSCOPE.

FIGURE 2.

exactly a third of those patients survived five years, — slightly higher than average.

It is clear that the cancer must be discovered before symptoms develop. Fortunately, two thirds of all the cancers of the large bowel are located within range of sigmoidoscopic examination and nearly 50 per cent are located within reach of the examining finger (Fig. 2). Consequently, a high measure of control of cancer of the colon and rectum could be achieved if digital and sigmoidoscopic examination were prophylactic routine, and the advice of the physician were followed after examination.

Operative Mortality

There has been a progressive and significant fall in the death rate in cases of resection of the colon and rectum (Fig. 3). In general terms, the operative mortality following resection for cure was about 15 per cent in 1937 and the years immediately preceding; it fell to about 9 per cent from the years 1939 to 1942 and to about 3 per cent from 1944 to 1948. These periods correspond so closely to the dark, middle and modern ages of chemotherapy that the advent of antibiotics must be considered the most important factor in mortality reduction. Adequate blood replacement, improved anesthesia, better intestinal decompression and more effective postoperative care are not to be minimized but in our opinion are less significant.

Definition of the Anatomic Segments of the Colon

The divisions of the colon have been more or less arbitrary, varying with various authors. This is particularly true of the rectum and sigmoid. Following the distinction of Gilchrist and David, we have used the term "extraperitoneal rectum" to refer to that portion of the rectum that is located entirely beneath the peritoneal floor. This is easy

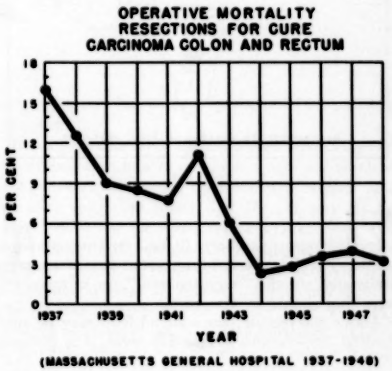

FIGURE 3.

to determine at the time of operation, and the upper level of the extraperitoneal rectum usually corresponds to a distance of approximately 8–12 cm. from the dentate margin, as observed by sigmoidoscopy. The "intraperitoneal rectum" comprises that area of bowel extending from the peritoneal floor approximately to the sacral promontory, where the colon becomes entirely surrounded by peritoneum, except for the thin mesenteric attachment that is common to the remainder of the colon. The transition from a wide posterior attachment with numerous blood vessels to a thin mesentery marks the

transition from intraperitoneal rectum to sigmoid. It is usually easy to determine at the time of operation but impossible otherwise, and corresponds to a level of approximately 20 cm. on the sigmoidoscope. The intraperitoneal rectum has often been designated as the "rectosigmoid," an unfortunate term that should be discarded.

Above the rectum, the sigmoid loop may be subdivided into various areas. However, it is difficult to distinguish the low sigmoid from the intraperitoneal rectum unless resection is carried out. Lesions in the midsigmoid and high sigmoid are easy to identify, either preoperatively by the barium enema or at the time of operation. The "left colon" in the statistical tables includes the descending colon and the splenic flexure. The transverse colon extends from just proximal to the splenic flexure to just distal to the hepatic. The right colon comprises the hepatic flexure, the ascending colon and the cecum. The distribution in each portion of the colon is shown in Figure 4.

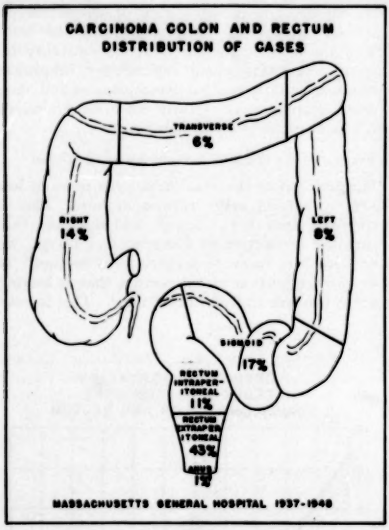

FIGURE 4.

Prognosis in Relation to the Level of the Lesion

According to a number of previous studies, including one of our own (Allen and Welch[11]), it has seemed that the prognosis has been better after resection of carcinoma of the right than of the left colon. Moreover, various studies have been made that indicate that the prognosis varies with the level of the carcinoma in the rectum and sigmoid, the lowest lesions having the lowest percentage of cure.

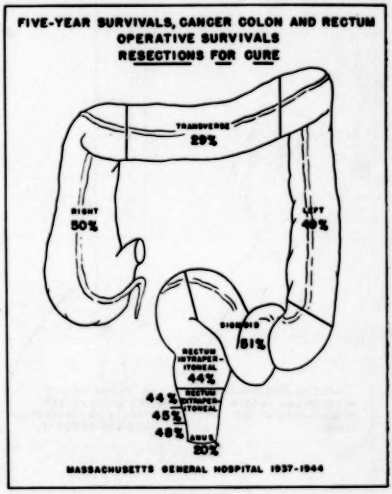

FIGURE 5.

TABLE 2. *Carcinoma of Colon and Rectum (5-Year Survivals — 1937-1944).*

	PERCENTAGE OF TOTAL CASES SEEN	PERCENTAGE OF OPERATIVE SURVIVALS, RESECTION FOR CURE
Right	26	50
Transverse	15	29
Left	24	49
Sigmoid	28	51
Rectum, intraperitoneal	25	44
Rectum, extraperitoneal	27	45
Anus	19	20
All cases	26	45

In this study, the outstanding feature is that there is no significant difference between the various locations of carcinoma with regard to five-year survivals, with the exception of the transverse colon and anus, which show poor survival rates. Thus (Table 2) the over-all five-year survival rate was 26 per cent for the right colon, 24 per cent for the

left colon, 28 per cent for the sigmoid, 25 per cent for the intraperitoneal rectum and 27 per cent for the extraperitoneal rectum as compared with 15 per cent for the transverse colon and 19 per cent for epidermoid carcinoma of the anus. Based on operative survivals after resections for cure, these figures become respectively (Fig. 5) 50 per cent for the right colon, 29 per cent for the transverse, 49 per cent for the left colon, 51 per cent for the sigmoid, 44 per cent for the intraperitoneal rectum, 45 per cent for the extraperitoneal rectum and 20 per cent for the anus. Since very few cases of carcinoma of the anus are encountered, this figure must be considered to be only approximate. The reason for the poor prognosis in carcinoma of the transverse colon is the fact that it is often impossible to obtain an adequate resection of the regional

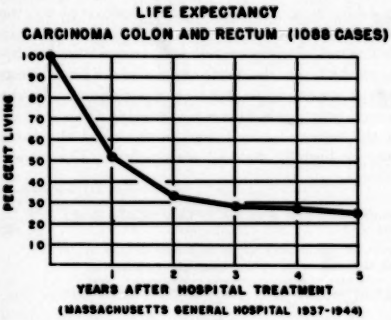

FIGURE 6.

lymph nodes, since the transverse mesocolon may be very short. With carcinoma of the anus the number of cases is small, but rapid metastasis to the groin has often made wide gland dissection necessary and has cut down the survival rate.

The prognosis in cancer of the extraperitoneal rectum has been investigated by dividing the rectum into three levels. The low rectum was arbitrarily defined as the area ranging up to 2 cm. above the mucocutaneous margin, the midrectum as 2½ to 7½ cm. above, and the high rectum as 8 cm. or more above, but the lower level of the cancer was below the peritoneal floor at the time of operation. The operative survivals of resections for cure had a five-year survival rate of 48 per cent for the low rectum, 45 per cent for the midrectum and 44 per cent for the high rectum. Corresponding percentages for the intraperitoneal rectum are 44 per cent and for the sigmoid, 51 per cent. Our figures suggest that there is no significant difference, therefore, in the prognosis for cases of cancer at the various levels of the extraperitoneal and intraperitoneal rectum.

The length of life following admission for all patients that entered the hospital from 1937 to 1944 is shown in Figure 6. Fifty per cent of all patients were dead slightly more than a year after entry. Two years after onset only 33 per cent were alive,

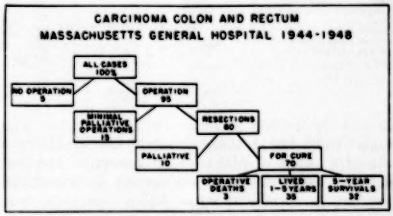

FIGURE 7.

and five years after entry 26 per cent of all patients were alive.

It may be estimated that a higher percentage of all patients that now enter the hospital will be alive in five years, since the operability is higher and operative mortality lower now than it was in the years 1937–1944. A hypothetical graph, using the resectability and operative mortality of the last five-year period, 1944–1948, and the survival rate determined in years 1937–1944, is shown in Figure 7. The approximate figure of 32 per cent five-year survival obviously will not be determined exactly until 1954, when the next group of survivals will be studied.

Lymph-Node Metastasis, Blood-Vessel Invasion and Prognosis

Carcinoma of the colon and rectum spreads by local extension, lymph-node metastasis or blood-borne metastasis. The importance of local extension, either by perforation of the bowel and involvement of contiguous structures or by growth along the lymphatics in the bowel wall, has been stressed sufficiently by other authors. Removal of portions of other viscera involved by direct extension has been done frequently. Allen,[12] whose cases are included in this study, found that he excised parts of other organs in almost exactly a third of all patients. Unfortunately, a somewhat less aggressive

attack has been employed by some surgeons. The local lesion was resected in 72 per cent of the cases in 1937–1943, and in 81 per cent of the cases in 1944–1948 (Table 3).

The determination of blood-vessel invasion requires serial sections for careful study, and in the present series of cases no conclusion can be drawn.

TABLE 3. *Carcinoma of Colon and Rectum.*

	TOTAL RESECTABILITY (CURATIVE AND PALLIATIVE)	
	1937–1943	1944–1948
	%	%
Right	69	75
Transverse	68	69
Left	71	86
Sigmoid	70	84
Rectum, intraperitoneal	75	84
Rectum, extraperitoneal	74	82
Anus	75	100
All cases	72	81

Sunderland[13] found the veins invaded in 27.6 per cent of a series of 210 cases of cancer of the rectum and sigmoid. In rectal cancer, he found the five-year survival rate after Miles' operation was 73.2 per cent without vascular invasion and only 41.4 per cent with it.

The presence of lymph-node metastasis has a similar bearing on the prognosis. In the present series, if no lymph nodes were involved 55 per cent of the patients who survived resection for cure survived five years (Table 4). When metastases were found, the corresponding figure was only 26 per cent. It appears, therefore, that the presence of lymphatic or vascular invasion reduces the prognosis after resection by approximately half.

TABLE 4. *Carcinoma of Colon and Rectum — Five-Year Survival Rates of Resection for Cure (Massachusetts General Hospital), 1937–1944.**

	NO METASTASIS			LYMPH-NODE METASTASIS		
	TOTAL CASES	FIVE-YEAR SURVIVAL	PERCENTAGE	TOTAL CASES	FIVE-YEAR SURVIVAL	PERCENTAGE
Right	50	30	60	26	9	35
Transverse	18	6	33	15	4	27
Left	32	16	50	9	3	33
Sigmoid	74	42	57	17	7	41
Rectum, intraperitoneal	46	25	54	27	4	15
Rectum, extraperitoneal	184	104	58	94	22	23
Totals	404	223	55	188	49	26

*Operative deaths, cases with missing pathological reports and obstructive resections that showed only gangrene on section are excluded.

Ulcerative Colitis

The development of carcinoma in a bowel previously affected by ulcerative colitis is extremely serious. Fourteen cases were found in this study. Of the entire group only 6 survived a radical resection, and only 1 was living free of disease at the end of the year. This emphasizes the fact that the only means by which this particular carcinoma can be controlled is prophylactic colectomy before malignant disease is established.

Polyps

The relation of benign polyps of the colon and rectum to carcinoma has been well established, and it is recognized that all such polyps should be removed. Whenever a satisfactory view of the polyp can be obtained through the sigmoidoscope, it is customary to destroy it by electrocoagulation if the polyp is located in either the rectum or the low sigmoid. However, if the polyp is above this level or in the sigmoid where its base cannot be seen accurately, colotomy, with polypectomy, and resuture of the bowel have usually been carried out.

The incidence of polyps of the colon, particularly in specimens resected for cancer, is high. Probably about 2 per cent of the normal population have undiscovered polyps, according to data collected by various cancer-detection centers. In our series of cancer of the colon and rectum, one or more polyps in addition to the cancer were discovered by the pathologist in nearly 20 per cent of the cases. In this series, 3 different clinical groups can be distinguished. In the first, one or two adenomatous polyps are found in the resected specimen. In the second polyps are numerous, ranging from 5 to 20 in the removed bowel, and in the third the colon may be literally covered with polyps. The second group is usually termed polyposis coli; the third is typical of familial polyposis.

When only 1 or 2 concomitant polyps are found, we have been unable to demonstrate that carcinoma tends to develop more frequently in the postoperative years. On the other hand, when polyps are numerous or familial polyposis is present, there is a greatly increased chance of the development of other carcinomas after removal of the primary lesion. Nearly all our patients with extensive polyposis have been treated too conservatively. The usual course has, therefore, been death from a second cancer. The proper treatment for this group is colectomy. The rectum should be sacrificed as well, unless there is only an occasional polyp that can

be destroyed effectively by electrocoagulation in a co-operative patient who will return frequently for follow-up.

Another group of patients that furnishes much interest has single polyps of the colon or rectum. According to Cattell[14] and Buie,[15] 80 per cent of these polyps occur in the rectum and distal sigmoid. In this particular paper, our interest is directed particularly to those polyps that on excision were found to contain carcinoma. There were 18 of these cases with a microscopical diagnosis varying from carcinoma in situ to adenocarcinoma, Grade II (Table 5).

The lesions were treated in two ways. The first group, usually poor-risk patients, had electrocoagulation or local excision. There were 12 of them; results were excellent in 10, but in the other 2 there was prompt recurrence, followed by a radical abdominoperineal operation and death from cancer within two years. The second group had, after excision or biopsy, an immediate radical resection. There were 6 in this group. All had rectal polyps, all had abdominoperineal resections and none had involved lymph nodes. All survived five years, but 1 died in the sixth year of metastatic cancer of the liver.

TABLE 5. *Single Polyps of Colon and Rectum, Massachusetts General Hospital, 1937–1944.*

	TOTAL CASES	DEATHS DUE TO CANCER
Local excision; final report: cancer	18	3
Immediate radical operation	6	1
Radical operation after local recurrence	2	2
No local recurrence	10	0

Although this series is small, it emphasizes the fact that these polyps cannot be treated locally without hazard. In a poor-risk patient local excision may be indicated, with the expectation that recurrence or metastatic disease will be noted at a later date in about 20 per cent of these cases. Early recurrence after local excision is a poor prognostic factor, and a radical operation is indicated immediately. The low incidence of local metastasis in this group gives some comfort to those surgeons who would save sphincters in these particular cases.

McLanahan,[16] in a study of 27 polyps of the rectum that demonstrated carcinoma on microscopical examination, came to the conclusion that local excision would be followed by recurrence in nearly a quarter of the cases. He pointed out the necessity of repeated biopsies throughout the entire specimen, and particularly at the base, with prompt radical operation if the base were involved or if recurrence developed.

When the polyp is found at a higher level in the bowel where a laparotomy is required for its demonstration, there now seems to be little reason to advocate a colotomy and polypectomy, particularly since resections and anastomoses can be accomplished with such a low mortality, recognizing the fact that the pathologist in some cases will make a final diagnosis of carcinoma in lesions that he will call benign at the operating table. Castleman states that inspection of the gross lesion and frozen sections cannot be relied on for differentiation of benign and malignant polyps. It is of interest that in the past six months in our hospital (Table 6), 37 single polyps of colon and rectum were removed that were believed to be benign at the time of excision. However, 5 were found to contain cancer in the final sections, and in one case lymph-node metastasis was found at a secondary resection. Even though the pedicle is long in many of these carcinomatous polyps, the surgeon who does a local excision high in the colon where the base cannot be followed by direct observation is bound to be unhappy. If the principle of bowel resection, including an adequate V of mesentery, be followed for these lesions, a more adequate operation for early carcinoma of the colon will result.

TABLE 6. *Single Polyps of Colon and Rectum, Massachusetts General Hospital, January 1–June 1, 1950.*

	TOTAL CASES
Preoperative diagnosis: benign polyp	37
Final diagnosis: carcinoma	5
Secondary resection performed	3
Lymph-node metastasis present	1

Multiple Tumors

Patients who survive resection of a cancer of the colon are more likely to develop a second carcinoma of the colon than normal persons. Of the 281 patients who survived resection for cure from 1937 to 1944, 7 later developed a secondary cancer in another portion of the bowel. This is an incidence of 2.5 per cent, approximately 100 times the incidence of cancer of the large bowel in the general population. One patient had 7 separate cancers of the colon and rectum over a period of fifteen years, and finally succumbed to liver metastasis. Two or more carcinomas of the colon and rectum were found simultaneously in 1 per cent of the cases; one patient had 4 separate carcinomas at the same time.

Choice of Operative Procedure

The aim of the surgeon is to accomplish a curative operation for cancer, preferably in one stage. This usually can be accomplished in patients with nonobstructed, nonperforated tumors by resection and primary anastomosis if the lesion is proximal to the rectum. In the presence of obstruction or perfora-

tion, decompression or defunctioning of the colon must be carried out before the resection. A more detailed discussion of the technic is beyond the scope of this paper but has been published elsewhere. There is, however, general agreement concerning treatment of carcinoma of the right and transverse colon. Since there are divergent views about the remainder of the colon, the choice of operation for cancer in the various portions of the colon supplied by the inferior mesenteric artery and for cancer of the rectum will be considered more fully.

Left Colectomy

Theoretically, three levels of nodes in the colon are available for removal, together with the primary lesion. In the left colon these comprise the pericolic nodes, the nodes along the branches of the inferior mesenteric artery and those along the inferior mesenteric artery itself. It has been the custom in the past to section the superior hemorrhoidal artery with resections of the rectum and low sigmoid, the sigmoid artery with cancers of the sigmoid, and the left colic artery with the splenic flexure, but it has been suggested that a more adequate left colectomy could be obtained if the entire inferior mesenteric artery were removed together with its terminal branches and the left colic, sigmoid, and superior hemorrhoidal arteries with accompanying lymph nodes. Such an operation would involve an extensive resection of the left colon and anastomosis of the midtransverse colon with the rectum near the peritoneal floor, and might conceivably increase the survival rate. Some indication of the necessity of this operation may be determined from a study of our cases.

In our series, of the patients who survived resections for cure and in whom the presence or absence of lymph nodes was noted, 205 had carcinoma of the splenic flexure, descending colon, sigmoid or intraperitoneal rectum in the years 1937–1944 (Table 3). Of these patients, 152 are known to have had no lymph-node metastasis. For them, the more extensive operation would have furnished no extra insurance of cure. Of the 53 patients who had metastasis to the nodes, the best percentage survival that could be expected would be that of the patients with nodes that were not involved, that is, 55 per cent. In other words, 29 patients theoretically could have survived if all involved lymph nodes could have been excised. Actually, 14 did live five years, so it is conceivable that 15 more patients might have lived after more extensive dissections. But to save this same group the more extensive operation would have been necessary in 205 patients, and it is probable that the postoperative complications in this group would largely, if not totally, counterbalance the gain.

It seems, therefore, that the performance of a left colectomy, including excision of the entire inferior mesenteric and its branches, is not justified as a routine procedure. However, if definite metastatic nodes are observed by the pathologist when the specimen is removed, it would be well to remove the entire artery, together with surrounding lymph nodes.

Rectum

A choice of methods is open to the surgeon when he deals with carcinoma of the intraperitoneal rectum, for here he may perform either resection and anastomosis or an abdominoperineal resection. If the carcinoma arises in the extraperitoneal rectum, an abdominoperineal resection is indicated except under most unusual circumstances.

During the period 1937–1944, resections and anastomoses of tumors of the intraperitoneal rectum or low sigmoid were carried out in 25 patients. In only a few instances did the anastomosis involve the extraperitoneal rectum. Within the last five-year period resection and anastomosis was carried out more frequently, and in many cases the suture line was placed low in the extraperitoneal rectum.

Enthusiasm for low anastomoses increased with the advent of antibiotics, which made them technically satisfactory procedures, but further experience has witnessed a decline in their popularity. We have encountered local recurrence when the bowel has been cut less than 5 cm. below the lesion (and this is 5 cm. judged by the pathologist rather than by the surgeon, who produces extra length by tension). In certain instances the recurrence has been of such a nature as to suggest local implantation in the suture line at the time of operation. This is not surprising, considering the excessive manipulation of the growth that is necessary when it is resected. Local recurrence has not been amenable to secondary abdominoperineal excision.

Even if 5 cm. of normal bowel may be obtained below the lesion, if obvious metastatic nodes are encountered it is wise to perform an abdominoperineal resection, since under these circumstances retrograde lymphatic metastases may occur. Occasionally, however, a low anastomosis may be carried out with less normal bowel below the lesion, as, for instance, after resection for large sessile adenomatous polyps or after palliative resection if there are extensive hepatic metastases.

In the 73 patients with carcinoma of the intraperitoneal rectum treated between 1937 and 1944, there was no significant difference in the survival rate according to the method of treatment. Twenty-five patients had resection and anastomosis with the expectation of cure and survived operation; 12 or 48 per cent were living five years later. Thirty-six had an abdominoperineal resection with five-year survivals in 14, or 39 per cent. Twelve were treated by a Hartmann operation (resection of intraperitoneal rectum and lower sigmoid, inversion of rectal stump and permanent sigmoid colostomy), with survival in 5, or 42 per cent.

Discussion and Summary

There is no need to disguise our disappointment in the figures that we have presented. They are neither so good as we expected them to be nor so good as they ought to be. They are persuasive enough, however, to indicate that the trend of therapy should be toward more radical procedures rather than toward conservative local excisions or sphincter-saving operations.

It is essential to obtain some standard method of comparison of the results of treatment in various centers. Now that large numbers of these cases are appearing, it seems best to judge results on the basis of all cases that are seen with the disease, whether operable or not. A clinical rather than a cytologic diagnosis will have to be accepted in many.

To compare the results in patients who are treated surgically, a second group can be singled out — those who were operated on with removal of all gross disease and who survived operation. Under any circumstances, patients who are lost should be counted as dead of disease. Furthermore, those dead of intercurrent disease should be classed, unqualified, as dead of cancer. By these means two simple, significant lists of figures may be obtained that can be compared in different clinics.

Our over-all figures indicate that 77 per cent of the patients who entered the hospital with cancer of the colon and rectum from 1937 to 1948 had resection of the involved bowel. The resectability has increased from 72 per cent in 1937–1944 to 81 per cent in 1944–1948. Five-year survivals were obtained in only 25 per cent of the total observed from 1937 to 1944. If the results are calculated on the basis of operative survivals with resections for cure, 45 per cent survived the five-year period. There is great variation of the latter figure, depending particularly on whether or not lymph nodes are involved (55 per cent when they are not involved; 26 per cent when metastases are present). Five-year survival rates were nearly identical in various sections of the bowel except for the transverse colon and for epidermoid carcinoma of the anus, in which areas they were lower.

Of the various changes in accepted surgical technics that should be advised, the following seem to be the most important: Prophylactic colectomy in ulcerative colitis and multiple polyposis is the only known method of control of the disease and should be advised more frequently. Polyps of the rectum or low sigmoid may be treated by fulguration through the sigmoidoscope when the pedicle is long and benign. If after a polyp has been removed through the sigmoidoscope the pathologist returns a diagnosis of cancer, a radical operation should usually be performed. A resection of a segment of the colon and mesentery should be done when the polyp is in the sigmoid or higher. Complete left colectomy is required if metastatic nodes are encountered during a resection for cancer of the sigmoid or left colon. Otherwise, the inferior mesenteric artery need not be removed. Resections of tumors of the lower sigmoid and intraperitoneal rectum with anastomosis should not be carried out unless at least 5 cm. of normal bowel and pericolic tissue can be obtained below the tumor. Resection and anastomosis of the extraperitoneal rectum is rarely indicated.

The outstanding fact is that nearly two thirds of all patients with cancer of the colon and rectum are incurable when they reach the hospital. Deaths from this disease cannot be reduced by further improvement in operative technic, since mortality is now so low that no significant gain can be expected in this respect in the larger clinics. In smaller hospitals, it is probable that the mortality is still too high and operability too low. Further control of the disease will depend on routine proctosigmoidoscopy as an integral portion of the physical examination, to discover the disease before symptoms are manifest, and prompt treatment by well trained surgeons.

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CLINICAL AND EPIDEMIOLOGIC OBSERVATIONS OF COXSACKIE-VIRUS INFECTION*

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COXSACKIE virus was first identified during a study of five small outbreaks of poliomyelitis in New York during the summer of 1947.[1, 2] The first strains were isolated from two paralyzed boys in the village of Coxsackie. The other epidemics in New York that year did not yield Coxsackie virus, but a number of isolations, including a second serologic type, were made later from specimens collected during the summer of 1947 in Wilmington, Delaware. During 1948 and 1949 the search was widened in New York and 24 isolations were made, including additional types and a second variety, Coxsackie virus Group B.[3] The present report is a summary of the clinical and epidemiologic observations made during these three years. The data are derived largely from the records of 517 patients whose feces were tested for pathogenicity for suckling mice. Thirty-three of these specimens were collected during 1947, 154 in 1948 and 330 during 1949 from large and small epidemics of poliomyelitis and from a few sporadic cases that occurred or were hospitalized in various areas in New York; 30 cases from Wilmington are included.

Methods

The methods used for the preparation of specimens during 1948 and 1949 differed only in minor details from those employed in the original studies.[2] Mice of the Albany standard strain, preferably two to four days old, were used. In order to assure a fair distribution of animals, the litters were pooled and then distributed by random sampling[4] to cages containing individual mothers. One half of a large litter or a complete litter was inoculated intracerebrally with 0.02 ml. of fecal suspension, and the other half of the litter, or a second family, was inoculated intraperitoneally with 0.05 ml. of the same suspension. In certain instances suckling hamsters and 10-gm. to 12-gm. mice were also inoculated.

Clinical Characteristics

The usual symptoms and signs of the patients who have been examined for the presence of virus have been headache, stiff neck or spine, fever of brief duration and cerebrospinal-fluid pleocytosis. Upper-respiratory infection or gastrointestinal symptoms preceded the onset of headache and muscle pain and spasm in many cases. None of the patients had symptoms suggestive of epidemic pleurodynia. Various analyses of the data have been made in an effort to differentiate the symptoms of patients who did or did not excrete Coxsackie virus. Paralysis of some weeks' duration occurred in 9 of the 30 proved cases (30 per cent) and in 180 (37 per cent) of the 487 cases from which virus was not isolated. Cerebrospinal-fluid pleocytosis was frequent in both the proved and the Coxsackie-negative cases. Thus the groups did not differ materially in either respect.

It may be noted that, if the proved cases be subdivided into Group-A and Group-B infections, there were 22 in A, of which 14 were paralyzed, and 8 in B, none of which were paralyzed. This difference is statistically significant, since the probability of a similar distribution on the basis of chance alone is not greater than 0.002.

Frequency of Isolation of Coxsackie Virus and of Paralysis

The frequency of isolation of Coxsackie virus and the frequency of paralysis by year are shown in Table 1. Of the 517 cases tested, 30, or 5.8 per cent, yielded virus. The percentage of specimens that contained virus was greatest in 1947 and least in 1949. As the figures indicate, there is an inverse relation between the frequency of isolation of Coxsackie virus and the frequency of paralysis by year. If such a difference occurred consistently it would afford one means of distinguishing between poliomyelitis epidemics that are and those that are not complicated by the presence of Coxsackie-virus infection.

Failure to Isolate Coxsackie Virus from Specimens Other than Feces

Howitt has reported the presence of Coxsackie virus in blood and cerebrospinal fluid and human tissues.[5] Of 74 cerebrospinal-fluid specimens examined during 1948 and of 13 in 1949, none yielded Coxsackie virus, although fecal virus was isolated from 3 of the patients. Sixty-nine blood specimens have been tested in suckling mice without satisfactory evidence of the presence of virus. Three of these were taken from positive cases. To date, Coxsackie virus has not been isolated from tissues collected from fatal poliomyelitis cases in New York State.

It may be well to mention one case in which Coxsackie virus was detected in mice that had been inoculated with a blood specimen. The case has been excluded from the other isolations because it was impossible to repeat the recovery and the

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original container was cracked when received and may have been contaminated. The patient's feces were negative. The case deserves mention because of its unusual clinical manifestations. The patient was a ten-year-old boy who lived at a State school. He complained of sore throat, anorexia and nausea for one day before he entered the hospital on July 15, 1948. He was admitted five hours after he had suddenly fallen down, and was unable to stand or move his legs because of extreme spasm and pain. His neck was stiff and his temperature was 103°F., but his spinal fluid was normal. Four hours after admission all signs of spasm and hyperesthesia had disappeared and the patient was again able to stand. Twelve hours later he became afebrile and otherwise normal on physical examination. Many of the boys had walked to and from a parade in the village near their school on July 5, and a number of them had purchased food at various concessions. The patient was among them, and was known to have stayed for part of the time with another boy who developed similar symptoms at the same time. The two were not close friends, and did not play together frequently. Feces and blood of the second boy were examined, but Coxsackie virus was not isolated.

TABLE 1. *Frequency of Isolation of Coxsackie Virus and of Paralysis.*

YEAR	NO. OF FECAL SPECIMENS TESTED FOR COXSACKIE VIRUS	NO. OF TESTED SPECIMENS THAT YIELDED VIRUS	PERCENTAGE OF TESTED SPECIMENS THAT YIELDED VIRUS	NO. OF COXSACKIE-NEGATIVE PATIENTS WHO WERE PARALYZED	PERCENTAGE OF PARALYZED PATIENTS
1947	33	6	18.12	3	11.1
1948	154	14	9.09	31	22.1
1949	330	10	3.03	146	45.6
Totals	517	30	5.8	180	36.9

Age Distribution

Comparison has been made of the age distribution of the Coxsackie-positive and Coxsackie-negative cases. The results are listed in Table 2, and indicate that the positive cases are more frequent in the youngest age groups. Seventy-three per cent of the patients with proved cases were less than 10 years of age. Fifty-one per cent of the negative cases fell in this group. Only 1 of the 30 patients with proved cases of Coxsackie-virus infection was more than 19 years of age.

TABLE 2. *Age Distribution of Coxsackie-Positive and Coxsackie-Negative Cases.*

AGE	POSITIVE CASES		NEGATIVE CASES	
	NO.	%	NO.	%
Less than 5	10	33.4	115	23.6
5 to 9	12	40.0	136	27.9
10 to 19	7	23.3	129	26.5
Over 19	1	3.3	93	19.1
Not known	0		14	2.9
Totals	30		487	

Sex Distribution

Twenty of the 30 proved cases were in males and 10 in females. Of the 487 Coxsackie-negative patients, 244 were males (50.1 per cent) and 241 were females (49.5 per cent). The sex of 2 is not known.

Geographic Distribution

Both groups have been tabulated according to residence. The results appear in Table 3. The only difference occurs in the higher percentage of proved cases from rural homes, but since the sample is small (3) it cannot be given much weight.

TABLE 3. *Positive and Negative Cases by Residence.*

TYPE OF CASE	RURAL (FARM OR CROSS-ROADS)	VILLAGE	CITIES OF 5,000 TO 25,000 POPULATION	CITIES OF OVER 25,000 POPULATION	TOTAL
Proved cases	3	10	6	8	27*
Percentage	11.1	37.3	22.3	33.3	100
Control cases	33	144	108	163	448
Percentage	7.3	32.1	24.2	36.4	100

*The records of 3 additional cases are unsatisfactory in this regard.

Distribution of the Several Types of Coxsackie Virus

Analyses have been made of the occurrence of Types 1, 2, 3[6] and untyped Group-A strains by years and place. The data that formed the basis for these calculations are listed in Table 4.

If these results are arranged in "2 x 2" tables and P calculated by the four-variable psi-function,[7] it may be shown to be highly improbable that the distribution of the several types by years is due to chance alone. The occurrence of different types in 1949 illustrates this. The table is as follows:

TABLE 4. *Number of Isolations of Various Strains.*

	GROUP A	TYPE 1	TYPE 2	TYPE 3	UNTYPED*	GROUP B
1947	6	3	3	0	0	0
1948	14	0	5	1	0	8
1949	10	3	0	0	7	0

*Untyped member of Group A distinct from Types 1-3. Preliminary studies on the 1949 specimens indicate the existence of 3 additional serologic types in this group, also distinct from Howitt's Types 4 and 5.

	UNTYPED	TYPED	TOTAL
1948	0	14	14
1949	7	3	10

P in this case is 0.000347, the odds being greater than 1 in 2800.

A similar analysis of the occurrence of Group-B strains also yields significant results. The data are as follows:

	GROUP B	NOT B	TOTAL
1947	0	6	6
1948	8	6	14
1949	0	10	10

Comparison of 1947 and 1948 gives P=0.0238. Comparison of 1948 and 1949 gives P=0.00408. Comparison of 1948 with both control years yields P=0.000513.

The absence of Type 1 in 1948 and its occurrence in 1947 and 1949 are also significant, but to a lesser degree. The other comparisons provide intermediate values that are nevertheless statistically significant. The three maps included in the present report illustrate these results (Fig. 1-3).

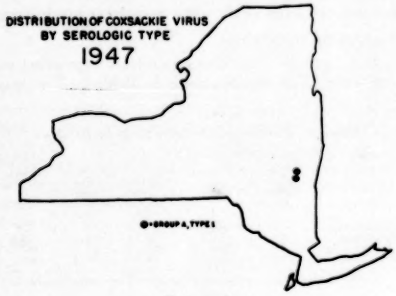

FIGURE 1.

Distribution by Month of Onset

Table 5 indicates the distribution of Coxsackie-positive and negative cases by month of onset. Only those months with a concentration of cases are shown. A few occurred at other times, but in many instances the circumstances were unusual, and in none was Coxsackie virus isolated. The Coxsackie-negative cases have also been shown according to presence or absence of paralysis. Such a comparison seemed of interest because of the observation of Gard[8] and Brøchner-Mortensen and Raaschou[9] concerning the seasonal distribution of paralytic and nonparalytic cases of poliomyelitis and the studies of Curnen, Shaw and Melnick of Coxsackie-virus infection in Connecticut in the summer of 1948.[10] In these reports evidence was presented of a different seasonal distribution of the paralytic and nonparalytic illnesses. Our own data suggest only that the isolation of Coxsackie viruses and the incidence of nonparalytic disease occurred most often during the poliomyelitis season.

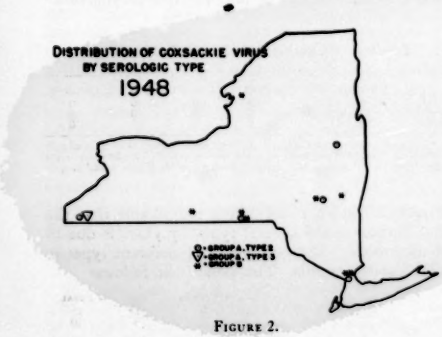

FIGURE 2.

DISCUSSION

The results leave little doubt that Coxsackie viruses may frequently be present in the feces of patients with symptoms of poliomyelitis. A number of other workers have made similar observations.[10-17] Whether this association depends in part on a larger sampling of poliomyelitis patients is unknown. The circumstances under which Coxsackie virus was initially found have doubtless prompted such sampling. The viruses have also been recovered from individuals with varied symptoms. Several investigators have associated infection with epidemic pleurodynia or Bornholm disease.[11, 14-20]

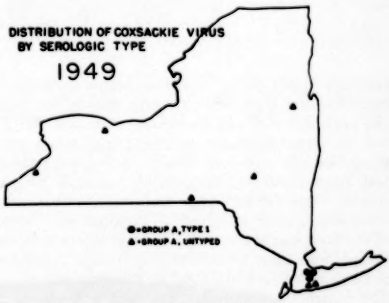

FIGURE 3.

In addition, various less distinct illnesses have been related to Coxsackie-virus infection. Howitt reported isolations from outbreaks of "three-day fever" and influenza-like illnesses.[5] Kilbourne has described a variety of manifestations simulating several diseases.[21] Thus there is nothing essential in the association of Coxsackie infection and poliomyelitis. In our own experience we have on three occasions isolated Coxsackie viruses from small outbreaks of summer illnesses that had been considered peculiar on clinical grounds by experienced physicians. On the other hand, we can hardly overlook the evidence, accumulated by many work-

ers, that although poliomyelitis infection is also extremely common relatively few cases are recognizable clinically. Some cases may be subclinical, but others may be atypical. The latter group is still imperfectly defined.

The failure to differentiate the clinical manifestations of the "poliomyelitis" patients in whom virus could and could not be found is obvious. A reasonable explanation would be that the Coxsackie infection contributed so little to the clinical symptoms that its effect was not evident.

If the inverse relation between incidence of paralysis and Coxsackie-virus infection holds, one would be tempted to suspect an interference. Interferences between viruses have been chiefly studied in the laboratory, but it is reasonable to look for them in nature.[22] It is too early to evaluate the experimental studies of interferences between poliomyelitis and Coxsackie viruses.[12, 23, 24]

The particular virus strain may need to be considered. The absence of paralysis among our Group-B infections may be a clue. Group B includes the Conn. 5 strain that was associated solely with nonparalytic cases in 1948. It may be noted that Group-B infections occurred that year in Connecticut, New York City and upstate New York. The three outbreaks were independently investigated. In all three paralysis was absent. In our experience Group-A strains have appeared in both severe and mild cases. On the other hand, Huebner, Armstrong, Beeman and Cole's cases were exclusively mild in nature.[25] All their strains were members of Group A.

The present epidemiologic observations imply that Coxsackie-virus infection is most common in the young. Seventy-three per cent of our cases were less than 10 years of age. We have tabulated the ages of the individuals from whom Coxsackie viruses have been isolated by others[10, 14, 16, 25, 26] according to their published reports and correspondence. Twenty-three, or 62 per cent, of the 37 cases were younger than 10 years of age. The sample is not large, but it suggests that infection elsewhere, as well as in New York, is predominantly of the young. Since the experimental disease is selective for immature animals, one is tempted to think of physiologic factors. It is more likely, however, that widespread immunization in nature accounts for the age distribution. Thus we have noted that the older members of families of persons with known cases may show humoral antibodies when the young siblings do not. Moreover, two pools of random adult serums included in many of our virus neutralization tests have been found to have antibodies for all types of Coxsackie virus we have so far encountered.

Our cases show a preponderance of males that is even more marked than that noted by Curnen in his presumptive cases. However, the 16 isolations reported by others in which the sex of the patients is mentioned show a still greater preponderance of males, the ratio being 3:1, whereas in our cases the figures are 2:1.

The evidence concerning seasonal distribution is suggestive but inconclusive. Our own cases have coincided with those of poliomyelitis. This may have been due to the manner of sampling. However, it should be noted that the largest number of Howitt's cases also occurred during August and September.[8] She reported a second, smaller peak in March, due to an outbreak in a military base. The cases reported by Curnen, Shaw and Melnick occurred during the poliomyelitis season, but evidence was secured of a significant difference in the times of peak incidence.[10] This was inferred from a comparison of the occurrence of paralytic and nonparalytic cases by months. The outbreak reported by Huebner and others occurred during July.[25] The population under observation was retested for the presence of virus in December and during the following summer, but no further isolations were made. The Ontario, Texas, Minnesota and Ohio cases also occurred during the poliomyelitis season.

The analyses of the probable significance of the occurrence of the various strains of virus require little comment. It is apparent that, within the limitations of our data, particular strains have not occurred in a given place or time in a purely random manner but were somehow influenced by self-limiting epidemiologic characteristics. The only type that was found in successive years was Type 2; in that

TABLE 5. *Distribution by Month of Onset.*

GROUP	MONTH						TOTAL
	JUNE	JULY	AUGUST	SEPTEMBER	OCTOBER	NOVEMBER	
Coxsackie positive	0	3	14	10	3		30
Percentage	0	10	47	33	10		
Coxsackie negative	7	67	217	98	48	12	449
Percentage	1.5	14.9	48.4	21.8	10.7	2.7	
With paralysis*	2	27	82	27	17	8	163
Percentage	0.6	16.5	51	16.5	10.5	4.9	
Without paralysis	5	40	135	71	31	4	286
Percentage	1.7	14	47.2	24.8	10.8	1.5	

*The classification of cases with paralysis is based on the patients from whom Coxsackie viruses were not isolated.

case there was a considerable geographic separation, namely, Delaware and New York.

Conclusions

Analysis of the results of a three-year study of the occurrence of Coxsackie virus among "poliomyelitis" patients suggests that infection is most common in young children and during the late summer months. The clinical records of "poliomyelitis" patients from whom Coxsackie viruses were isolated did not differ materially from the records of patients from whom virus was not isolated. Statistically significant differences have been found in the distribution by time and place of the several types of virus. Coxsackie virus has been found as frequently in the feces of paralytic as in those of nonparalytic poliomyelitis patients. An inverse relation between frequency of paralysis and frequency of isolation of Coxsackie viruses has been noted during the years 1947 to 1949.

Note

Dr. E. G. Weisenburn of Coxsackie, New York, who had attended the two 1947 Coxsackie-virus patients, reported the following year that he had seen a number of children in Coxsackie with headache, nausea, muscle pains and fever. None were paralyzed. One of these patients, a six-year-old girl (D. J.), was visited August 5. The girl complained of a sore throat and headache and nausea when active. Nothing was discovered by physical examination. Her axillary temperature was 100°F. A specimen of feces proved to be infectious for suckling mice and a Group-B strain of Coxsackie virus was isolated.

An outbreak of "about 20 cases" was observed by Dr. Richard W. Rice of Johnson City, New York, during the first week of August, 1948. Only 3 patients were hospitalized, and only 1 case was seriously considered to be poliomyelitis. The common symptom was headache. Half the patients complained of muscle pains; the rest, of nausea and vomiting. Recovery was rapid (within forty-eight hours) in all but 3, although a number reported weakness and fatigue that persisted for as long as two weeks.

Five patients were studied for the presence of Coxsackie virus. Their ages were 8 years (3 patients) and 11 years (2 patients). A Group A, Type 2 virus was isolated from one. Three of these children, including the one with a proved case, were known to have been in close contact, and 4 became ill on the same day. The fifth had become ill on the previous day. Stiff neck and back were noted in each case. The cerebrospinal fluid was examined in 3 cases. In one (the child from whom virus was isolated) 7 cells per cubic millimeter were found on the fourth day of illness; 13 cells per cubic millimeter were found two days later. The second child's cerebrospinal fluid contained 5 lymphocytes. The fluid of the third child contained 246 cells on the fourth day (70 per cent being polymorphonuclear leukocytes and the rest lymphocytes), 300 cells on the sixth day (95 per cent being lymphocytes) and 15 cells on the fourteenth day.

A somewhat similar report was received later in the month from Dr. I. J. Rosefsky of Binghamton, New York, not far from Johnson City. A number of children were observed with a rather characteristic illness. The major symptom was stiffness of the neck, in Doctor Rosefsky's reports a "steppage nuchal rigidity," a rigidity that appeared on beginning flexion of the neck and then disappeared only to return when the flexion was continued. The ages of the 4 children from whom specimens were submitted were 4 (2 cases), 5 and 6 years. From one of these (C. M.) a Group-B virus was isolated. This child lived in a neighborhood in which a number of children became ill at the same time. Muscle pains were noted in C. M., but there was no paralysis. Cerebrospinal fluid was drawn from 2 of the 4 children. One of the specimens was contaminated. The second, drawn on the day of onset, did not show pleocytosis. It seems probable that in these cases, as in those in Johnson City, the explosive nature of the outbreak and the absence of more severe symptoms drew attention to them.

We are greatly indebted to William R. Thompson, Ph.D., for the statistical analyses and to Dr. George Boines of Wilmington for clinical records and for a variety of specimens. The 1947 fecal specimens were received through the kindness of Miss Beatrice Howitt of the Communicable Disease Center, United States Public Health Service, and Dr. Robert Ward of the College of Medicine, New York University.

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ACUTE MEDIASTINAL EMPHYSEMA COMPLICATING ECLAMPSIA*

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CINCINNATI

THE occurrence of acute mediastinal emphysema during labor and delivery is an unusual and sometimes puzzling complication. Numerous case reports of this entity have been described during the past fifty years, but simultaneously occurring convulsive eclampsia was noted in only a few instances. The incidence of this complication seems to have decreased (if case reports in the literature may be used as an index) during the last fifteen years, probably as a result of improvements in analgesia, anesthesia and "prophylactic" forceps.

Gordon[1] in 1927 noted that the midwife Louise Bourgeois, attending the Queen of France in 1617, recognized the condition and described adequate prophylaxis: "I saw that she tried to stop crying out, and I implored her not to stop, for fear that her throat would swell." Kosmak[2] in 1905 reported one case and was able to find 77 cases in a review of the literature. Gordon[1] presented two cases in 1927 and reviewed 50 additional ones, describing them under the title "Respiratory emphysema in labor." Most cases occurred in young primigravidas. Only 2 of these 130 reported patients died, an autopsy on one revealing rupture of the pulmonary alveoli with air beneath the pleura but no emphysema of cellular tissues. Gordon outlined a pathophysiologic mechanism and suggested that the air reached the mediastinum via subpleural dissection to the root of the lung, then through the sheaths of the great vessels. Subsequent extensive experimental and clinical investigation proved his assumption correct. Since 1930, however, cases presenting this entity have been meager in the obstetrical literature, and most recent reports of such cases have appeared in thoracic, pediatric and internal medical publications.

Hamman[3] in 1934 described 3 cases of interstitial disease of the lungs, later employing the term "spontaneous mediastinal emphysema." Numerous case reports (under the title of Hamman's disease) followed, particularly in association with infectious diseases, atelectasis of the newborn, asthma and intratracheal anesthesia. The following case is believed to be of interest because of the extreme degree of mediastinal and subcutaneous emphysema that was superimposed on convulsive eclampsia.

CASE REPORT

H. M. (Unit No. 166,298), a 21-year-old unmarried, unregistered primigravida, entered the Cincinnati General Hospital on December 23, 1947, in a state of deep coma. A meager history was obtainable from the patient's mother, who denied any previous knowledge of her daughter's pregnancy. The patient had complained of mild abdominal cramps and headache twenty-four hours prior to admission but had taken no medication. One hour prior to admission she was found by her mother to be comatose, sprawled in a pool of blood on the cellar floor, with a stillborn fetus nearby. The lifesaving squad severed the umbilical cord and brought the patient to the hospital. The fetal size was consistent with a gestation of thirty-six weeks.

Physical examination revealed a well developed, well nourished woman, who appeared desperately ill. She was comatose and did not respond to questioning or stimuli. The pulse was 160, the temperature 101.4°F., the respirations 44 and the blood pressure 144/108. Respirations were stertorous and there was profuse froth about the mouth. The tongue was bitten and edematous and partially blocked her airway. Marked fetor oris was present. Severe acne of the face, chest and back was noted. The face and neck were edematous, the lips cyanotic, the hands and feet cold and livid. A marked crackling subcutaneous emphysema was evident over the right and left chest and back, as far down as

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the costal margin. It extended upward through the neck and face as high as the temples. The head was pulled to the right and could not be moved. The right pupil was larger than the left, and both reacted sluggishly to light and accommodation. The fundi were normal. Chest expansion was equal bilaterally. Bilateral basal rales were heard. There was no evidence of rib fracture. The breasts were full; adhesive-tape strips had been placed over both nipples. The heart was not enlarged to percussion. The sounds were not heard distinctly because of respiratory noises. There was normal sinus rhythm with a rate of 160. There were no murmurs. The blood pressure revealed a pulsus paradoxus. On the abdomen was seen a well healed right rectus scar. Peristalsis was normal. The reflexes were ++++ over the biceps, triceps and radial tendons. The Hoffmann test was positive on the right; knee jerks and ankle jerks were ++++; the Babinski and Oppenheim signs were positive on the right. There was no evidence of motor paralysis. The uterus was firm at the level of the umbilicus. The pubic area was covered with dried blood and the umbilical cord protruded from the vagina. Inspection of the labia, introitus and vagina revealed only minimal abrasions. Vaginal bleeding was moderate.

Analysis of the urine revealed a ++++ albumin, with 5 to 6 granular casts per high-power field. Tests for acetone and sugar were negative. The blood urea nitrogen was 17 mg., the carbon-dioxide combining power 31 vol. and the uric acid 7.3 mg. per 100 cc.; the chloride was 538 mg. Examination of the blood revealed a hemoglobin of 14.5 gm. with a red-cell count of 3,500,000 and a white-cell count of 13,000. Lumbar puncture, between the 4th and 5th lumbar vertebras, with poor relaxation and under an initial pressure of 110 mm., yielded 4 cc. of clear, Pandy-negative fluid with a protein of 64.5 mg. per 100 cc. Microscopical examination revealed 4 lymphocytes, 2 polymorphonuclear leukocytes and 12 red cells per high-power field.

Course. Shortly after admission the patient appeared moribund, the pulse mounting to 170 and the blood pressure being unobtainable. The heart sounds were distant. The skin temperature was cold and the extremities cyanotic. No convulsions had been seen, but because of the edematous, chewed tongue, marked albuminuria, stillborn fetus, hyperuricemia and acidosis a diagnosis of fulminating eclampsia was made. Cerebral hemorrhage was considered in the differential diagnosis, as was particulate-matter pulmonary embolism. The subcutaneous emphysema was believed to be due either to a ruptured pulmonary alveolus or bleb from extreme expulsive efforts of delivery or to gas-bacillus septicemia from self-induced labor.

Treatment. The placenta was expressed by suprafundic pressure; vaginal bleeding was minimal. An intravenous infusion of 1000 cc. of a 5 per cent solution of glucose in water was started, in conjunction with a massive intravenous injection of penicillin. Oxygen was given by mask, suction of the mucus from the nose and mouth was accomplished and the patient was catheterized, 40 cc. of concentrated urine being obtained. She was given 10 cc. of a 50 per cent solution of magnesium sulfate by deep intramuscular injection, 0.003 gm. of atropine and 0.09 gm. of papaverine. One hour later the blood pressure had mounted again to 144/108 and the pulse was 130. Another liter of the 5 per cent solution of glucose in water was administered, together with 4 drops of Veratrone,* given hypodermically. The blood pressure promptly fell to 110/80 and the pulse to 92. The pressure was controlled at this level with 3 drops of Veratrone, given hypodermically every two hours, and 5 cc. of the 50 per cent solution of magnesium sulfate, injected intramuscularly every six hours.

Immediate puerperium. Under the treatment outlined above the blood pressure and pulse were well stabilized and urinary output was adequate. No convulsions occurred. However, three hours after admission the patient was still comatose. Physical examination at this time revealed total absence of the heart sounds, and cardiac dullness could not be elicited. A diagnosis of progressive mediastinal emphysema was made. This was confirmed by x-ray films of the chest: ". . .there is extensive mediastinal emphysema with extension into the neck and paravertebral space." Progressive venous distention and elevated venous pressure developed, and surgical consultation was obtained. However, over the next few hours cardiac tamponade did not develop and mediastinotomy was not deemed necessary. An ear, nose and throat consultant also saw the patient because of the progressive edema of the tongue and pharynx and the spreading emphysema. Emergency tracheotomy equipment was kept at hand but was not utilized.

A characteristic precordial "crunch" that was synchronous with systole became evident on the first post-partum day. The heart sounds were faint, but minimal cardiac dullness could be distinguished. The urinary output was 325 cc. during the first twenty-four hours of hospitalization. On the second day the patient was able to answer questions but was totally disoriented and amnesic. The precordial "crunch" was still present, and bilateral shoulder pain developed. Subcutaneous emphysema was unchanged, and the urinary output mounted to 1650 cc. per twenty-four hours. The blood urea nitrogen rose to 38 mg. and the uric acid dropped to 4 mg. per 100 cc. The patient's general condition improved during the next four days. By the seventh post-partum day most of the subcutaneous emphysema had dissipated, the heart sounds were normal, the mediastinal emphysema had disappeared radiologically and the blood urea nitrogen was normal. The hypertension and albuminuria continued, however, until the twelfth post-partum day. Kidney-function tests performed at this time were all within normal range, and the patient was discharged on the sixteenth day.

Review of the past history before discharge revealed only measles, mumps and chicken pox in childhood and an appendectomy at the age of 11. There was no history of pulmonary tuberculosis, heart disease, hypertension, kidney disease, rheumatic fever, chorea or previous convulsive episodes.

Follow-up: It had been noted that the patient appeared extremely depressed and morose after the seventh day, at which time she became fully cognizant of the events that had preceded her hospitalization. Psychiatric examination disclosed an incomplete adjustment, and it was necessary later to place the patient in a mental institution, the diagnosis being schizophrenia. Follow-up studies showed normal blood pressure and urinalyses.

*Parke-Davis preparation of veratrum viride.

Discussion

Certain predisposing and precipitating factors necessary for the development of mediastinal emphysema have been classified by Aisner and Franco[4] into the following groups: atelectasis with associated alveolar ectasia, such as pneumonia, pertussis, asthma, inhalation of foreign bodies and atelectasis of the newborn; increased intra-alveolar pressure resulting from forceful respiratory efforts against pressure, such as parturition, straining, laryngospasm, playing wind instruments; tracheal insufflation, such as intratracheal anesthesia, resuscitation of newborn, positive-pressure inhalation therapy. Usually more than one factor is in operation, together with certain intrinsic tissue deficiency or congenital deformity.

The pathological physiology involves rupture of alveoli of the marginal type, that is, those adjacent to bronchi, vasculature, septa or pleura, with diffusion of air into connective-tissue spaces and along sheaths of the pulmonary vessels giving rise to pulmonary interstitial emphysema and, if pressure gradients are sufficient, spread to the mediastinum. Pneumothorax may result from rupture of the mediastinum if the pressure is excessive, or from rupture of a subpleural bleb. Air may ascend from the

mediastinum into the neck, head, chest and occasionally even into the extremities or retroperitoneal areas.

The most common symptoms associated with this entity are: chest pain, usually sudden and severe, precordial or substernal, with occasional radiation to the left arm or shoulder; dyspnea, due either to altered pulmonary function resulting from the interstitial emphysema or to altered circulatory function because of collapse of the pulmonary vessels or increased mediastinal pressure resulting in diminished venous return, a true cardiac "tamponade"; cyanosis; palpitation; or anxiety.

The diagnosis of mediastinal emphysema is usually not difficult. The sudden appearance of subcutaneous emphysema in the region of the neck and head, either with or without pneumothorax, is suggestive evidence. Progressive diminution in the heart sounds, decrease or obliteration of cardiac dullness and the appearance of the typical "mediastinal crunch," a bizarre sound synchronous with systole, will usually suffice for diagnosis. A careful history of such predisposing factors as are listed above should be taken. Electrocardiograms are of value in only about a quarter of the cases, and no specific pattern has been demonstrated. X-ray examination will usually reveal the air pattern but occasionally serial films will be necessary, and lateral views should always be included. It is important, especially in the recent parturient, to distinguish the disease from pulmonary embolism, pericarditis, myocardial infarction and mediastinitis.

Treatment consists mainly of supportive measures, but in the face of increasing mediastinal pressure with cardiac tamponade, mediastinotomy has proved to be of great value.

Summary and Conclusions

A case of acute mediastinal emphysema complicating eclampsia in a recent parturient is presented.

This disease, an unusual complication of labor and delivery, seems to have become rarer during the past twenty years, is more common in the young primigravida and has a good prognosis.

A summary of the disease process is outlined.

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CLINICAL NOTE

AN UNEXPECTED ULTRA-VIOLET RAY BURN RECEIVED IN AN UNUSUAL MANNER*

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A sixty-seven-year old man was admitted to the Boston City Hospital Skin Clinic with a complaint of intense burning over the lower back and upper buttocks. He gave a history of stopping at a rest room in a bus station, where ultraviolet-ray germicidal tubes are used in connection with rest-room sanitation (Fig. 1). He sat on the toilet approximately ten or twelve minutes, at the end of which time he noted burning and tingling of his back. That night he had considerable discomfort and was unable to lie on his back. Physical examination on the following day of the lower back and upper buttocks showed a skin that was brilliantly red, with a few scattered vesicles (Fig. 2). On palpation the skin was very tender. The skin covered by his shirt escaped injury. Under soothing treatment the condition was relieved in a few days.

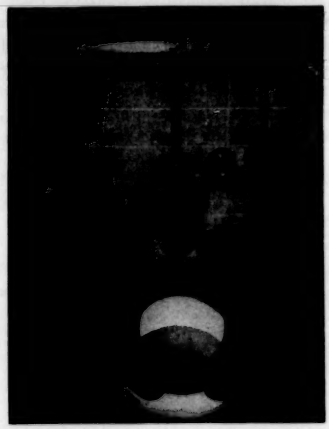

FIGURE 1. *Toilet with Hood Housing Ultraviolet-Ray Tube. Light is constant, not cutting off when toilet is in use.*

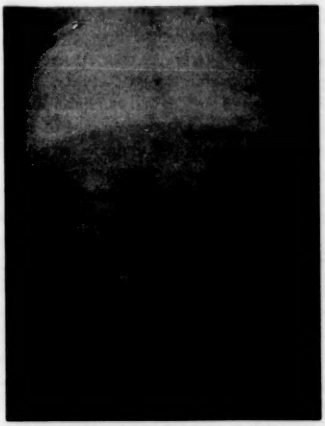

FIGURE 2. *Erythema and Vesiculation Noted on the Day after Exposure to Ultraviolet Ray.*

CONCLUSION

It is suggested that the company manufacturing these lights devise some method of disconnecting the current while the toilet is in use.

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MEDICAL PROGRESS

THE MANAGEMENT OF ACUTE FRONTAL SINUSITIS

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THE purpose of this paper is to review the recent trends in the control of acute bacterial infections of the frontal sinus consequent to the impact on therapeutic concepts of the bacteriostatic and bactericidal agents during the last decade. The results in the field of otolaryngology have been so dramatic in reducing the complications of upper-respiratory infections requiring surgery that there is a widespread belief that the "wonder drugs" have supplanted all previous methods of treatment. One has only to remember the prevalence of surgical mastoiditis before the advent of chemotherapy and to compare that era with the present day to be acutely aware of this revolution. But although it is true that the number of cases in otology and rhinology that require surgery has markedly decreased and that dangerous intracranial and systemic complications have all but disappeared from the scene, the fact remains that the human race is still as susceptible as formerly to infections of the upper-respiratory tract caused by viruses and bacteria. Actually, the new drugs have not changed the fundamental picture of sinus disease at all; they are merely a new and more effective weapon to use in its control. Inasmuch as they have altered and masked the signs and symptoms encountered in the natural course of the disease, it is appropriate to review the clinical picture of untreated acute sinusitis.

In the first place, one should recognize that there are all degrees of severity of infection of the paranasal sinuses. This variation depends on the susceptibility of the individual, his diathesis to respiratory infection, the virulence and type of the infecting organism, complicating factors such as anatomic variations in the nose, the presence of nasal polyps, allergic reactions that cause nasal obstruction during an acute infection and various forms of trauma. The usual history is that the patient "catches a cold." Usually the patient cannot distinguish this cold from the so-called common cold at the onset, but within a few hours the inflammation will have spread through the mucosa to the ostium of one of the sinuses or possibly to the ostia of all the sinuses — in the case of the frontal sinus, to the nasofrontal duct. If to this infection trauma is added, such as exposure to cold wind, the inhalation of water while swimming or physical violence, the infection may progress rapidly to one of the complications, such as meningitis, brain abscess, septicemia or osteomyelitis of the frontal bone. But the infection may be confined to the ostium of the sinuses. In such a case, the patient may experience some pain due to the sudden closure of the sinus, the absorption of air within the sinus producing the condition known as vacuum pain or headache. This same mechanism is present in the aerosinusitis due to a sudden alteration of atmospheric pressure incident to changes in altitude while flying, except that in this latter circumstance the symptoms are more sudden and violent. In this stage, the patient has the usual symptoms of an early acute respiratory infection: malaise, chilly sensations followed by rise of temperature and a stinging sensation in the nose, followed soon after by a profuse discharge. This stage is followed by the appearance of leukocytes, which soon change the secretion from a mucoserous to a mucopurulent discharge. If the mucosa of the sinus cavity has not been involved in the infection, the disease may last for a very few days and no consequent damage will have been done to the lining of the sinus. However, if the infection passes through the ostium and involves the sinus cavity the sinus mucosa becomes swollen with inflammatory edema, and pus accumulates within the sinus. The latter will either drain into the nose or remain within the cavity depending on the patency of the natural opening. In such a case the patient suffers intense pain, tenderness over the sinus at critical points and frequently a throbbing, pounding headache increased by motion of the head and on leaning forward. There is an accompanying rise in temperature and a polymorphonuclear leukocytosis. At first the pain may be constant throughout the twenty-four hours. As the infection subsides, it is characteristically experienced at regular hours of the day; usually the pain appears in the forenoon, increases in severity and disappears by midafternoon. This periodicity recurs day after day until the inflammation has subsided. In children and in patients who have not been subject to previous infections of the sinus, the onset of the first attack may be characterized by inflammatory edema of the eyelids and the adjacent areas of the face.

Prior to the advent of chemotherapy, the most effective treatment consisted of complete rest in bed; the application of heat to the sinus — either a hot-water bottle, heating pad or infra-red lamp;

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the avoidance of drafts; the use of sedation for pain and at the proper time gentle shrinking of the mucous membrane of the nose to promote drainage. In regard to the latter, too early and too vigorous application of the vasoconstricting agents would only serve to irritate the nose and destroy all benefit of the physiologic action of the nasal cilia, and usually resulted in a very sore nostril and minimal opening and draining of the sinus. However, as the acute stage of the inflammatory edema begins to subside, the local application of a shrinking solution at the ostium of the sinus will open it sufficiently to allow the escape of the retained purulent secretion. This often is under some pressure; hence a free flow of pus commonly follows the withdrawal of the nasal applicator. This shrinking solution may also be applied by means of an atomizer, which is especially useful if the patient must apply the medications himself. At this stage, if drainage was not accomplished by these methods some surgical interference of a minor nature was resorted to. This consisted of infracting the middle turbinate; that is to say, in some cases in which the middle turbinate is so close against the ostium of the sinus that it is a mechanical obstruction to drainage, the insertion of a flat blunt periosteal elevator between the turbinate and the ostium and the breaking away of the tip of the turbinate by forcing it away from the ostium will allow the sinus to drain. If this is not successful, a trephine of the sinus may be necessary. This, then, is the clinical picture of an acute infection of the sinus without the use of the antibacterial drugs; in most cases in which this procedure is carried out conscientiously the patient completely recovers in two to four weeks.

Factors that prevent recovery are a badly deviated septum, a middle turbinate pressed against the ostium, a nasal polyp blocking the same region or a frontoethmoidal cell that narrows the nasofrontal duct so that the lumen of the duct is too narrow for drainage of the frontal sinus. Complete recovery may also be hindered by the patient's occupation, the economic necessity for his returning to work before recovery is complete, exposure to bad weather, as in the case of sailors and men working on outdoor engineering construction, or trauma from inhaling noxious fumes and dust while at work.

The extension of the disease to adjacent structures is always to be feared. An undrained ethmoid or frontal sinus may perforate through the thin orbital wall and produce an orbital abscess, or if there has been previous disease and the present illness represents an acute exacerbation there may be extension through a thinned-out posterior frontal sinus wall, with the production of an extradural abscess. Trauma to an infected frontal sinus may still produce osteomyelitis and fulminating disease with extension to the meninges and brain. At any time during the process septicemia may occur.

The course of the disease has been greatly altered since the advent of chemotherapy and antibiotics, but because of a tendency to use these agents in a hit-or-miss fashion the clinicopathological picture of the disease is frequently lost sight of. Patients too often return to work as soon as their temperature has returned to normal and the pain has disappeared, although they still may have severe infection that is masked by the effects of the drug. Moreover, because of the dramatic response to these drugs there is great reluctance on the part of the patient to stop work. "Give me a shot of penicillin, because I have a lot of work to do" is a phrase heard too often. It is true that many are able to continue working during an attack, due to the relief afforded by one of these drugs, but the toxicity of the infection is still present and there is continuing absorption of toxic products by the body as a whole. Such a patient feels unusually fatigued or may complain of muscular aches or inability to carry on a day's work as usual or may begin the day energetically but be "all in" after a few hours. In other words, the toxicity of the infection has not been controlled.

Nevertheless, antibiotics are of tremendous value in shortening the duration of sinus infection. The course of an attack is certainly shortened (in many cases it is reduced from three or four weeks to a matter of days) by early and adequate dosage carried out until all signs and symptoms of the disease have cleared up, but in addition to early and adequate dosage one should nevertheless insist on the earlier supportive measures, such as bed rest, that were employed prior to the discovery of these drugs. To repeat, masking of the disease is the greatest pitfall of antibiotic treatment.

The selectivity of action of these drugs makes us seek a more accurate diagnosis and identification of the causative agent of sinusitis to gain more specific control of the disease. Prior to their discovery, determination of the bacteria involved was frequently of academic interest only. Whether it was a streptococcus, a pneumococcus, or a staphylococcus that caused the infection did not materially alter the prescribed course of treatment. It was more terrifying, of course, to realize, when intracranial complications occurred, that one was dealing with a pneumococcus. Bacteriologic studies put one on his guard in anticipation of other conditions such as septicemia, erysipelas, pneumonia and kidney complications.

The rhinologist can now obtain invaluable assistance from the bacteriologist. This is, in my opinion, the most important change in the therapeutic approach. If we know accurately the organism involved and its susceptibility to a specific antibiotic, we can treat the disease with greater certainty of success. Use of the shotgun approach, in the hope that a "wide-spectrum" antibiotic will catch the unknown organism, is not scientific. It may be necessary in an emergency, before cultures

have been reported, to give a patient one of the antibiotics, but it is extremely important to take a culture first, so that the therapeutic agent may be changed if necessary with a minimum of delay. Outstanding in this concept is the work of Davison,[1] who points out the relative insensitivity of gram-positive cocci to the action of penicillin at the present time as compared with their sensitivity as observed six years ago. For example, in 1945 he found 80 per cent of the strains cultured from his cases to be sensitive to 0.2 units per cc., whereas in 1949 only 12 per cent of such cultures were sensitive to this same concentration. He blames the widespread use of penicillin dust, nose drops and other inadequate methods of treatment, which have merely killed off the more sensitive organisms and allowed the resistant strains to survive. He agrees with the statement of Fleming,[2] who cautioned against the use of too small doses. Davison uses dihydro-streptomycin as well as large doses of penicillin in order to obtain maximum antibiotic activity. For a person weighing 150 pounds he prescribes procaine penicillin G, 300,000 units, combined with 100,000 units of crysticillin penicillin every three or six hours, depending on the severity of the infection. In addition he used dihydro-streptomycin, 0.7 gm. every twelve hours. He continued this treatment for seven to ten days. He states that this treatment program "has cleared up some long-standing chronic infections without operative treatment other than puncture and lavage of pus-filled antra." Presumably this would obtain in frontal-sinus infections as well. To determine the proper antibiotic he uses sensitivity cultures on blood-agar plates.

Here is a word of caution on the other side of the picture. Although the antibiotics may help to arrest and "cure" the infection, one should never overlook the fact that undrained pus requires evacuation. This is one of the oldest surgical principles. No amount of chemotherapy or penicillin will drain empyema of the frontal sinus if the nasofrontal duct remains blocked. The oldest operation for relief of frontal sinusitis was the trephine. This antedates all the other operations such as those of Killian, Jansen, Lynch and Lothrop and has been revived recently by Brown,[3] who states that if the patient's progress is not satisfactory under conservative therapy the trephine operation for drainage of the frontal sinus should be performed early, as he feels that irreversible damage will otherwise be caused to the mucosa of the sinus. He lists as indications for this procedure: persistent frontal pain, associated with fever, the presence of these symptoms after three or four hours indicating that adequate drainage has not been established by intranasal shrinkage; increasing edema over or under the sinus; moderate symptoms not responding to treatment after twenty-four hours; and acute exacerbations of a chronic frontal sinusitis. If swimming is the etiologic factor, earlier trephine is advisable. The procedure consists of a small supraorbital incision exposing the floor of the frontal sinus in its medial portion and the making of a small opening at this point into the sinus, not disturbing the lining membrane except at the site of the opening. The pus is evacuated and the sinus drained for a few days until the nasofrontal duct has regained its patency.

Except for the trephine of the sinus that fails to drain through conservative methods, it is generally considered unnecessary and even dangerous to operate on an acutely infected sinus. However, there are several conditions that arise in the course of an acute infection that necessitate early operation. As mentioned before, the infection may perforate the floor of the sinus and enter the orbit or may pass through bone previously thinned by chronic disease, as in the case of a pyocele, in which event no amount of nasal shrinkage is of any use. External incision and drainage is necessary, and where chronic changes already exist due to previous disease one of the more radical procedures may eventually be required to prevent a recurrence. If the extension of the disease leads to intracranial complication, again there is no benefit to be obtained from conservative local measures; surgery to ensure drainage of the extension, as in the case of an epidural or brain abscess, must be undertaken. In osteomyelitis, which we rarely see as an acute fulminating disease at the present time, and low-grade localized infection of the frontal bone secondary to infection or trauma of the sinus, surgery of a radical nature is still required at some time in the course of the acute disease.

So far, nothing has been said concerning the allergic sinus. The allergy incident to chronic sinus disease is not considered in this study of acute infection. It is well to bear in mind, however, that a patient may develop an acute bacterial infection of his sinuses in the course of an allergic rhinitis and that treatment must therefore be directed to both conditions.

No mention is made of the "common cold." This is a viral infection and unless it later becomes complicated by bacterial infection is self-limited. Nevertheless, one may be called on to care for such a case in the early stages. No treatment for such patients is more effective than bed rest, a minimum of local medication and only such symptomatic treatment, such as aspirin and sedatives, as will make the patient more comfortable.

Antihistamines seem of no use unless, as previously mentioned, an allergic rhinitis is also present. Much has been done recently to discourage the indiscriminate use of these agents by such investigators as Browning[4]; Lowell, Schiller, Alman and Mountain[5]; Cowan and Diehl[6]; Bloomfield[7]; Hoagland, Deitz, Myers and Cosand[8]; and Feller, Badger, Hodges, Jordan, Rammelkamp and Dingle.[9]

Conclusions

Chemotherapy and antibiotic drugs have revolutionized the field of sinus disease in so far as shortening the course of the disease and preventing many of the surgical complications are concerned. Greater knowledge of the bacterial aspects, such as the proper identification of the bacteria and a determination of their sensitivity to antibiotics aids in treating the disease more specifically and, therefore, more effectively, is desirable. Surgical complications are still possible and when present require appropriate and early operation. Except where there is an allergic factor complicating the disease, antihistamines would seem to offer no help.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

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CASE 37231

Presentation of Case

A thirty-eight-year-old blind woman was admitted to the hospital complaining of increasing girth of the abdomen, difficulty in breathing and left-upper-quadrant pain.

Eleven weeks before admission she had discovered prominent abdominal veins by palpation. Nausea and vomiting two to three times per day occurred with intermittent sharp interscapular pain. Bilateral ankle edema was observed, as well as a weight loss of twenty-five pounds from her usual 218 pounds. These difficulties led to an investigation in another hospital, where studies, including laryngoscopy, chest and abdominal x-ray examinations, an intravenous pyelogram and a basal metabolic rate, were reported as normal. A diagnosis of "nervousness" was made. After this, nausea and vomiting abated, thus contributing to a feeling of improvement, although marked weakness prevented the patient from easily accomplishing her usual household duties. Subsequent to an upper-respiratory infection three weeks before entry, gradual progressive abdominal swelling, aching in the left upper quadrant and increasing difficulty in breathing were first noticed. There had been an additional weight loss of 50 pounds. Because dyspnea became progressively worse and a sharp, nonlocalized, intermittent abdominal pain had begun, the patient was brought to the hospital.

Inquiry revealed no previous respiratory difficulty, precordial pain, limited exercise tolerance, jaundice, diarrhea, change in bowel habit, hematemesis or food intolerances. For severe chronic constipation the patient had always taken enemas. She had observed the presence of hemorrhoids for many years, but over the past year they had been a little more troublesome than usual. Regular menstrual periods until ten months prior to entry had been replaced by irregular and often missed periods, as well as occasional intermenstrual spotting. Profuse nonodorous vaginal discharge was also observed.

When the patient was ten years old one eye was punctured by a pencil. Infection occurred and was followed by sympathetic ophthalmia. Fifteen years prior to entry severe right-upper-quadrant pain was described as "gall-bladder colic." Whether jaundice was present or not is not known. At one time she worked for a man who had tuberculosis.

On physical examination the neck veins were not distended. Slight limitation of movement of the elevated diaphragm was observed. The heart and lungs were not remarkable except for a Grade I precordial systolic murmur. Over the distended, tense abdomen were prominent superficial veins around the umbilicus that extended cephalad onto the chest. Although the abdomen was generally tympanitic, shifting fluid dullness could be demonstrated. There was slight upper-abdominal tenderness bilaterally, with the nontender smooth-edged liver and tip of the spleen felt just below the costal margin. There was pitting edema of both legs. Rectal examination was negative. Vaginal examina-

tion was unremarkable except for a profuse whitish discharge, which seemed to arise from the os.

The temperature was 98.6°F., the pulse 96 and the respirations 20. The blood pressure was 160 systolic, 122 diastolic in both arms.

Laboratory studies revealed an acid, amber-colored urine, with a specific gravity of 1.005 to 1.008, and a + test for albumin; the sediment contained no red cells, 10 white cells, 6 to 12 epithelial cells, bacteria and a few trichomonas per high-power field. Blood studies showed a hemoglobin of 13.5 gm. and a white-cell count of 7600, with a normal differential. The stool was guaiac positive on admission but later was guaiac negative. The blood Hinton test was negative. The alkaline phosphatase was 7.3 mg., the fasting blood sugar 83 mg., the total protein 6.34 gm., the albumin 4.46 gm., the globulin 1.88 gm. (albumin-globulin ratio of 2.4), the nonprotein nitrogen 16 mg. and the total van den Bergh determination 0.6 mg. per 100 cc. The bromsulfalein retention was 28 per cent and the prothrombin time 27 seconds (normal, 19 seconds). The vaginal smear showed intracellular diplococci, but bacterial culture of the organism was negative for *Neisseria gonorrhoeae*. An x-ray film of the chest was not unusual and a plain film of the abdomen showed an enlarged liver; the lower splenic pole could not be positively identified. The barium-enema examination was unsatisfactory, but no obstruction was observed and no gross lesion was identified on the visualized left side. A gastrointestinal series showed no demonstrable esophageal varices or aberration in the stomach or duodenum. A large, firm, tender, rounded mass was subsequently felt in the left upper quadrant; it moved a little with respirations but could not be isolated definitely from either kidney or spleen. Retrograde pyelograms showed depression of the left kidney and a suggestion of some compression of the left upper calyx, but no frank invasion or elongation of the calyceal system was recognized (Fig. 1).

On the twentieth hospital day an operation was performed.

Differential Diagnosis

Dr. Joseph C. Aub*: "A diagnosis of 'nervousness' was made." Under the circumstances a diagnosis of "nervousness" was very risky.

I think the remark that she "worked for a man who had tuberculosis" is the type of phrase often put into the clinicopathological histories as a "red herring."

It puzzles me that this person with mortal disease was operated on.

May I see the x-ray films, please?

Dr. Stanley M. Wyman: No definite evidence of disease is seen in the x-ray films of the chest. One film from the barium-enema examination shows some depression of the distal transverse colon, but there is no evidence of localized intrinsic disease in the colon.

Dr. Aub: That does not fit in with the description in the record.

Dr. Wyman: It was reported as negative. I think that should be interpreted as meaning that no intrinsic disease was seen. The two films taken from the gastrointestinal examination show changes suggestive of some pressure on the lesser curvature of the stomach, but that is not definite. It may be displaced forward somewhat, but there is no intrinsic stomach disease.

Dr. Aub: They are miserable pyelograms, aren't they?

Dr. Wyman: She was a very heavy patient. I do not believe the description of the pyelogram is quite correct. I think there is definite compression of the upper calyxes (Fig. 1).

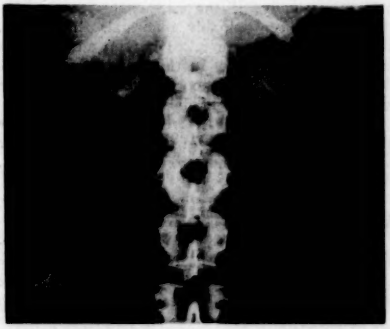

Figure 1.

Dr. Aub: This looks as if there was a mass over it.

Dr. Wyman: Very definitely. Most probably there is a large mass in the left upper abdomen that is pushing the kidney down, compressing the upper calyxes and perhaps pushing the stomach forward and the colon down. I think the spleen is located in this general vicinity. I cannot outline it very well.

Dr. Aub: Isn't that the mass here?

Dr. Wyman: Very possibly, Dr. Aub. The kidney is here. I cannot be too definite about it.

Dr. Aub: You think she had a hypernephroma, don't you?

Dr. Wyman: Yes.

Dr. Aub: In eleven weeks, this patient lost 75 pounds; therefore this was probably a malignant tumor. She had a mass that I suppose may have been a cyst, but I do not think anybody who had

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a pancreatic cyst would lose 75 pounds in eleven weeks. To account for the edema of the legs and for the fluid in the belly she must have had an obstruction. Since she had a normal serum protein with a normal albumin-globulin ratio it appears to have been an obstruction to the circulation, either in the vena cava or in the liver. The caput medusae meant that she had a mass obstructing the portal circulation in the liver. The pitting edema of the legs might come from a belly so full of fluid that tension was greater outside than inside the vena cava, which was thus obstructed. However, the description does not support this. The irregular menstrual periods and intermenstrual spotting I interpret as due to involvement of the liver — the liver was not destroying estrogen. That is one diagnosis the pathologist cannot say I am wrong about. Obviously the liver condition was recent, as nothing was found in the other hospital. She was studied quite thoroughly; if she had cirrhosis the liver should have been palpably abnormal. In addition, abdominal plates were taken but no mention was made of a large liver. In this hospital the bromsulfalein test showed poor excretion, and there were other signs of liver disease. If I have interpreted all these findings correctly, she had to have obstruction in the liver. In the x-ray film the liver was rather large, — not *very* large, was it, Dr. Wyman?

DR. WYMAN: It is very hard to outline well, Dr. Aub. I do not want to say very much about it.

DR. AUB: But the fact that she had a caput medusae is suggestive of a portal difficulty, so it may have been primary or secondary in the liver. I assume she had a neoplasm. There is no reason to go into any other discussion about that. She may have had one of three neoplasms: hepatoma with cirrhosis, hypernephroma or carcinoma of the body of the pancreas. To my way of thinking, that is the differential diagnosis. All three of these tumors affect the venous circulation, and the venous obstruction is the crux of this diagnosis.

If she had a hepatoma, it would have been in the left lobe of the liver. I have discussed this with Dr. Mallory. I think a great many hepatomas are on the left side, and he thinks that most of the hepatomas are on the right. This would have to have been in the left lobe of the liver. Hepatoma with a cirrhosis could produce a great many of the patient's symptoms, but she had a good deal of pain with it, the mass was very far over on the left side, and the examination in the other hospital ought to have indicated that something was wrong with the liver. Hepatomas readily invade the hepatic veins and may grow into the vena cava, obstructing it sufficiently to produce edema of the legs and also to produce a caput medusae. In that regard hepatoma is a perfectly satisfactory diagnosis. I do not think it was a hepatoma. It was in a peculiar position for a hepatoma, and the diagnosis ought to have been considered in the other hospital.

Secondly, it may have been a hypernephroma. Hypernephroma has the same characteristic of sticking its nose into the vena cava and obstructing return circulation in the vena cava. I must say these x-ray findings are much more suggestive of its being a hypernephroma than I thought they were when I read the record. She had a low urinary specific gravity and a few pus cells but no red cells in the sediment. She also had a hypertension that ought not to be present with hypernephroma but that might occur if a hypernephroma obstructed the venous flow on one side.

Thirdly, it may have been a carcinoma of the body of the pancreas. The diagnosis of tumor of the body of the pancreas is practically never made before operation or autopsy. It is a relatively rare disease; it is particularly rare in women, and the patient was rather young for it — thirty-eight years old. Tumor of the pancreas practically never occurs until the fifth decade. It causes pain, which this woman had, on the left side going up to the scapula, anorexia and most of the other symptoms that this woman complained of. How would it cause edema? In a high percentage of the few cases, venous thromboses occur not only in the splenic vein, where they are relatively common, but also in the liver and sometimes in the vena cava. The tumors are likely to lie directly over the vena cava and the aorta and may impinge on the vena cava and cause edema of the legs in that way. It would be hard to account for the caput medusae on the basis of carcinoma of the pancreas except by metastases to the liver, which readily occur. It also metastasizes very often to the lung and to the bone, which in this patient do not show anything. Carcinoma of the pancreas metastasizes widely. The pain this patient had was moderate for carcinoma of the body of the pancreas. The anorexia fits in, and also the bleeding, inasmuch as carcinoma of the pancreas metastasizes very rapidly to the lymph nodes around the stomach. The palpable masses that one feels in this disease are likely to be lymph nodes; the pancreas has a big lymphatic supply and metastases occur very rapidly.

One could discuss this for a long time, but I do not see any need for it. I think the diagnosis lies between a hypernephroma and a carcinoma of the pancreas. I made Dr. Wyman say what he thought it was. Just for the fun of it, I shall bet on the other diagnosis; it may have been either of the two. I shall say it was carcinoma of the body of the pancreas, that the mass that was felt did not move much because it was pancreatic, that it involved the vena cava sufficiently high, and that there were metastases in the liver sufficiently great to produce a caput medusae — although that is unusual for metastases. The patient had hypertension and she had white cells and a constantly low specific grav-

ity in the urine; therefore I think I shall have to say that she had a pyelonephritis. First, I think she had a carcinoma of the body of the pancreas, and secondly, she may have had a hypernephroma.

DR. JOHN T. QUINBY: Dr. Aub, do you think a retroperitoneal tumor, such as a leiomyosarcoma, could produce this picture by pressing on the vena cava and on the stomach, accounting for the low food intake?

DR. AUB: Yes; I meant to include that in the differential diagnosis, because it is possible that it was a retroperitoneal tumor, other than from the body of the pancreas, but my first bet is pancreas.

DR. JACOB LERMAN: The protocol does not actually express the difficulty we had in the differential diagnosis. When the patient first came in, the findings were localized to the liver and there was evidence of cirrhosis. We all felt a large mass in the right upper quadrant that extended across to the left side and was thought to be a large left lobe. Anyway, we believed that there was a large liver, due to some form of cirrhosis. Then our problem was to find the cause of the cirrhosis, which was not obvious. One of the students persisted in the opinion that the patient did not have an enlarged liver on the left but a mass distinct from the liver. Every day, when we arrived on the ward for rounds, he called our attention to the mass on the left side. Finally he convinced me that she had a mass in the left flank that was distinct from the liver and spleen and that did not move on deep respiration. Our attention was directed to the kidney, and a pyelogram was made. The pyelogram demonstrated a large mass in the left flank that depressed the kidney and deformed the calyxes. The service agreed with the radiologists that the deformities of the calyxes were important in the etiology, and they accepted a diagnosis of hypernephroma. Then the question came up: Why the clinical picture of cirrhosis? Did she have a separate cirrhotic involvement plus a hypernephroma, or was the hypernephroma the explanation of the entire condition? Were there metastases with invasion of the liver and invasion of the vena cava or perhaps invasion of the hepatic vein to account for the marked caput medusae and the extensive collateral circulation? Most of us thought that there was involvement of the liver by metastases and invasion of the portal circulation with obstruction of the splenic, the portal and probably the hepatic veins.

DR. AUB: Did the surgeons look for a hypernephroma? Did they operate from the rear?

DR. LERMAN: She was then transferred to the Genitourinary Service. There was some competition between the Surgical Service and Genitourinary Service concerning who would operate. We finally compromised, and both residents operated, by the thoracolumbar approach.

CLINICAL DIAGNOSIS

Hypernephroma.

DR. AUB'S DIAGNOSIS

Carcinoma of body of pancreas, with liver metastases; ?hypernephroma.

ANATOMICAL DIAGNOSIS

Renal-cell carcinoma with vena-caval and portal-vein obstruction.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: A very large tumor was found in the left kidney; it had invaded the capsule of the kidney and involved the surrounding peritoneal tissue. It had also grown, as renal carcinomas characteristically do, into the renal vein and extended along that into the vena cava. From the symptoms it seemed quite certain that it must have extended beyond the entrance of the splenic vein — and that proved to be the case. There was direct extension of the tumor into the porta hepatis so that it was impossible to be sure just where the portal vein was situated, although it was almost certainly obstructed by tumor. The caval involvement would not be at all unusual in this type of tumor, which sometimes grows directly into the right auricle, forming a huge auricular thrombosis, but the portal-vein obstruction by renal-cell carcinoma is distinctly unusual.

The nephrectomy was carried out, and the patient was able to leave the hospital but was forced to return in a little over a week because of further increase of the abdominal swelling.

A PHYSICIAN: Was any observation made of the state of the liver at operation?

DR. LERMAN: I was told that in addition to the extension of the tumor along the portal circulation one of the surgeons believed there was involvement of the liver itself.

CASE 37232

PRESENTATION OF CASE

First admission. A forty-one-year-old man was admitted to the hospital complaining of fever and night sweats.

About six weeks prior to entry he began to have copious night sweats that occurred at about 4:00 a.m. nightly. He found that his temperature was normal or slightly elevated during the day but rose to 102°F. or 103°F. every evening between 6:00 and 9:00 p.m. He was given daily injections of penicillin for an indefinite period, without effect on the fever. Four and a half weeks before entry he began to have shaking chills at the time of the

evening fever; the chills continued to recur for about one week. During this time he lost 24 pounds in weight, in spite of a normal appetite. He was again given penicillin, as well as Chloromycetin, for ten days without improvement. The medications were discontinued because of the development of urticaria across the shoulders. Streptomycin and aureomycin were given for two days without change, and no medications were given for ten days prior to admission. There were no associated symptoms. An x-ray film of the chest, blood culture and tests for undulant fever, malaria and tuberculosis were all said to have been negative. He had not drunk any well-water or unpasteurized milk. There had been no contact with animals other than a healthy Angora cat. He had not lived or traveled abroad or in the south.

The past history revealed that he had had asthma, usually in the fall, until the age of twenty. A "dermoid cyst" had been removed from the sacrum twelve or fifteen years ago. There had been no other serious illnesses or operations. At times in the past he had been a heavy drinker. During the early weeks of his illness he stated that he consumed as much as one fifth of a gallon of Scotch whisky daily, but none had been consumed for three weeks prior to admission here.

Physical examination revealed a well developed and nourished man. Two to three rubbery, movable, nontender lymph nodes were palpable in the right inguinal region, and a right epitrochlear lymph node was felt. The tip of the spleen was palpable. Rectal examination was negative.

Urinalysis was negative except for 8 red cells per high-power field in the sediment. Examination of the blood disclosed hemoglobin contents of 10.9 and 11.8 gm. and white-cell counts of 6700 and 6500, with 77 per cent neutrophils, 3 per cent large lymphocytes, 8 per cent small lymphocytes, 5 per cent monocytes, 7 per cent eosinophils and "somewhat increased" platelets. The sedimentation rate was 57 mm. in one hour. A blood Hinton test was negative. The serum nonprotein nitrogen was 23 mg. and the total protein 5.86 gm. per 100 cc., with an albumin-globulin ratio of 2.3. A bromsulfalein test showed 18 per cent retention forty-five minutes after injection of 5 mg. of dye per kg. of body weight, and a cephalin-flocculation test was negative after twenty-four and forty-eight hours. One blood culture showed *Staphylococcus albus* and 1, *Staphylococcus aureus*; 3 showed no growth. Agglutination for undulant fever was negative. A clear voided urine on culture showed a moderate growth of *Staphylococcus albus* and few alpha-hemolytic streptococci. The stools were guaiac negative, and no amebas were seen on one examination. An x-ray film of the abdomen demonstrated definite enlargement of the spleen and some enlargement of the liver. Intravenous pyelograms showed a normal urinary tract and several calcified densities in the right midabdomen, thought probably to be within lymph nodes. A cholecystogram and barium-enema examination were normal. A gastrointestinal series, including small-bowel studies, was normal except for a tiny hiatus hernia and moderately increased prominence of the rugal folds of the stomach, with some thickening of the stomach wall; peristalsis was normal and the stomach emptied well. An electrocardiogram was normal. A lateral film of the skull and an anteroposterior view of the dorsal spine were normal.

During the ten-day hospital course the patient felt well and had no chills; the sweats were much less severe. The temperature was never below 98°F. and there was a daily rise to between 99.2 and 101.4°F., the highest usually recorded between 7:00 and 11:00 p.m. He was discharged home on a high-carbohydrate, high-protein diet and ferrous sulfate.

Final admission (one month later). Three days after discharge the fever and night sweats returned to the previous degree, with a sensation of burning and flushing of the face and drenching sweats. There were no shaking chills. The peak of the fever had been occurring earlier in the day than was previously the case; that is, at about 7:00 to 8:00 p.m. Two weeks before entry the patient had entered another hospital, where an x-ray film of the chest, barium-enema examination, sinus films and cystogram were reported as normal. However, two physicians felt a mass in the right lower quadrant by simultaneous rectal-abdominal examination. The patient had gained 11 pounds since discharge but felt weak.

Physical examination revealed partial conduction deafness and a retracted drum in the right ear. A 0.5-cm. freely movable, firm, nontender lymph node was palpable at the lower end of the right posterior cervical chain, as was a left-axillary 1-cm. freely movable lymph node. The spleen was felt 1 fingerbreadth below the left costal margin on deep inspiration. There was a definite 3-cm. nontender, fixed mass just above the right pubis. There was an exquisitely tender spot along the course of the right spermatic cord. On rectal examination, a number of freely movable nodes could be felt, high on the right and posteriorly, outside the lumen of the bowel.

The urine had a specific gravity of 1.020 and gave a + test for albumin; the sediment contained 10 red cells per high-power field. Examination of the blood revealed a hemoglobin of 10.5 (and 11.4) gm. and a white-cell count of 4500, with 78 per cent neutrophils, 9 per cent lymphocytes, 7 per cent monocytes and 6 per cent eosinophils. A prothrombin time was 40 per cent of normal.

The lowest temperature recorded was 98.2°F. orally and the highest 103.2°F. orally.

On the third hospital day an operation was performed.

Differential Diagnosis

Dr. Reed Harwood*: The history up to the time the patient was discharged from the hospital the first time suggested some infectious process. Apparently the physicians could not make a diagnosis and sent him home because they did not know what to treat.

May I see the films?

Dr. Stanley M. Wyman: The spleen appears to be quite large, extending down almost to the iliac crest, and is very long and slender. The liver also extends downward quite a distance, although I am not so certain about liver enlargement as I am of spleen. Two films from the pyelogram show normal-appearing kidneys, and the calyceal systems seem quite normal. I am somewhat impressed by the right ureter's lying as far medially as it does.

Dr. Harwood: As far medially?

Dr. Wyman: It usually lies more laterally, more like the left ureter in this film, so I would wonder about something's displacing the ureter. The bones of the spine do not appear abnormal. Two films of the gall-bladder series seem normal, as does the examination of the colon.

Dr. Harwood: Was there a film of the chest?

Dr. Alfred Kranes: No film of the chest was taken here. A film that was taken elsewhere a few days before entry was normal.

Dr. Harwood: Not even slightly abnormal?

Dr. Kranes: Not even slightly!

Dr. Wyman: There is a single anteroposterior film of the thoracic spine that shows no definite abnormality. The films of the gastrointestinal series also were not remarkable.

Dr. Harwood: On the first admission, the patient had symptoms suggesting merely an acute infection, but by the time of the second admission a number of masses had appeared. A cervical lymph node was palpable, the spleen had become considerably larger in the interim, a group of lymph nodes were felt on rectal examination and a mass was felt in the lower part of the abdomen. I would place Hodgkin's disease as the most likely diagnosis to fit those findings in a person who had intermittent fever. I am going to read excerpts from a paper by Jackson and Parker,† because they discuss the diagnosis of Hodgkin's disease much better than I could:

> In the last analysis, the diagnosis of any type of Hodgkin's disease must rest on a properly executed biopsy. [I believe in this case the cervical node was biopsied.] It is true that in certain advanced cases of Hodgkin's granuloma with generalized lymphadenopathy, evidence of involvement of internal organs, fever, polymorphonuclear leukocytosis and anemia, the diagnosis can be made with some degree of assurance on clinical grounds alone, but even under these circumstances experience has taught us that we may be mistaken.
>
> We therefore advise the removal of a lymph node whenever feasible. The node must be selected with care and with due reference to any possible surgical risks. In all cases, a fair-sized node should be removed, for the small satellites toward the periphery of an involved area not infrequently show merely nonspecific inflammatory changes, and it is not easy to persuade a patient to submit to a second operation for no better reason than that the first one was unsatisfactory.

That may be the reason that the surgeons did not do a biopsy on the epitrochlear node on the first admission.

> When confronted with simple lymphadenopathy apparently confined to a single region, one must consider various forms of lymphoma, — that is, giant-follicle lymphoma, reticulum-cell sarcoma, lymphosarcoma, Hodgkin's paragranuloma and Hodgkin's sarcoma, — as well as tuberculosis, carcinoma, chronic inflammation, infectious mononucleosis, syphilis, leukemia and certain other conditions.

That is the list of the common conditions that may produce lymphadenopathy. For the sake of brevity I am not going to exclude them one by one but will simply state that for one reason or another I have excluded all but Hodgkin's disease.

> Fever may be the presenting symptom and indeed the only symptom for weeks or months, and this sign will later be discussed in detail. Its presence, particularly if it is relapsing in type and is not obviously due to one of the more usual causes, should rouse the suspicion of Hodgkin's disease. A careful search for enlarged lymph nodes, especially in the abdomen, should be made, and x-ray studies may reveal the presence of involvement of the mediastinum. [That is the reason I questioned Dr. Wyman and Dr. Kranes about the chest films.]
>
> One of our patients had a relapsing type of fever over a year prior to the development of any notable peripheral lymphadenopathy.
>
> The fever may be of various sorts. Most frequently it is, as Uddströmers puts it, typeless. Occasionally it is intermittent or remittent, reaching 101° to 105°F. every day. More rarely a high continuous fever is seen. Such a finding is almost always terminal. It is common knowledge that pyrexia becomes increasingly frequent as the disease advances.
>
> During febrile periods unassociated with sepsis, it is usual for the lymph nodes to increase in size; splenomegaly, if it exists, frequently becomes more marked, and the patient is generally prostrated, weak and debilitated.

— And as we have seen, this patient developed fever again as soon as he left the hospital; when he returned to the hospital many more lymph nodes were observed and the spleen was larger.

> There is a peculiar and characteristic reaction that deserves special attention—so-called Pel-Ebstein fever. In 1887 Pel and Ebstein independently described a relapsing form of fever characterized by periods of pyrexia, alternating with intervals during which the temperature is normal or subnormal. The febrile periods are marked by a gradual daily increase in temperature to 104°F. or more and a subsequent equally orderly decline to normal. The pulse and respirations usually follow the temperature in such a manner that when the latter is 104°F. the pulse is 120 to 150 and the respirations are 30 to 35. During the period of increased temperature, most patients feel extremely ill. There follows an afebrile period of weeks or months, during which the patient may return to apparently perfect health, but sooner or later the fever returns and the febrile intervals become shorter, and eventually the fever becomes continuous.

That ends my discussion.

Dr. Tracy B. Mallory: Is everyone willing to accept Dr. Harwood's diagnosis?

*Assistant physician, Massachusetts General Hospital.

†Jackson, H., Jr., and Parker, F., Jr. Hodgkin's disease. VI. Clinical diagnosis. *New Eng. J. Med.* 234:37-41, 1946.

Dr. John T. Quinby: I wonder whether he did not also have a good deal of hepatitis? He had justification for impaired liver function in his drinking habits, and he had a low serum protein.

Dr. Mallory: By "hepatitis" I assume you mean degenerative liver disease, not viral infection of the liver.

Dr. Quinby: Yes.

Dr. Kranes: Dr. Harwood is quite right in stating that we did not know what was going on at the time of the first admission. The patient came in to see if we could determine the cause of the fever, and we went through the usual diagnostic steps. The only abnormalities found were the anemia and the rapid sedimentation rate. Liver disease was considered, and one person thought it the most likely cause of the symptoms, but most of us thought that if he had any liver disease it was incidental. The reason the lymph nodes were not biopsied was that they were not impressive — they were no larger than those usually found in many people — and he was therefore discharged to the family physican for observation. We believed that something was bound to turn up sooner or later, and it did, much sooner than we anticipated. When he came in the second time, the mass in the lower part of the abdomen, which I felt rectally and Dr. Welch felt abdominally, was quite apparent. He was immediately turned over to the surgeons. A biopsy of the abdominal nodes rather than of the others was done because we believed that it would almost certainly yield a diagnosis and the others might not.

Clinical Diagnosis

Hodgkin's disease.

Dr. Harwood's Diagnosis

Hodgkin's disease.

Anatomical Diagnosis

Malignant lymphoma, Hodgkin's sarcoma type, of retroperitoneal lymph nodes.

Pathological Discussion

Dr. Mallory: Dr. Welch, will you tell us your findings at operation?

Dr. Claude E. Welch: The operation consisted of an exploratory laparotomy. We decided to remove the mass that was palpable. As the mass was low in the right lower quadrant the liver could not be biopsied, but it did appear normal on palpation and inspection. There was no cirrhosis. The only lymph nodes that were enlarged were located along the common iliac artery on the right. The node that we felt was about the size of an orange and was located close to the dome of the bladder; it was removed for biopsy.

Dr. Kranes: It should be mentioned that a cystogram was done in another hospital and was said to have been negative. It is too bad that the films are not available, as I think Dr. Welch would agree that they showed a very definite pressure defect on the right side.

Dr. Wyman: That is somewhat in keeping with the displacement of the right ureter.

Dr. Mallory: The section from the enlarged lymph node that Dr. Welch had removed showed complete destruction of the nodal architecture, some relatively large foci of necrosis and very numerous multinucleated cells of the Sternberg-Reed type, quite characteristic of the picture of Hodgkin's disease. There were so many of these big atypical cells, — and mitotic figures were so numerous, — that it was classified as the sarcomatous type of Hodgkin's disease. That classification is of importance only as regards prognosis. It makes it definitely poorer than it would be if it were the ordinary type of Hodgkin's granuloma.

Dr. Kranes, can you tell us anything about the subsequent course and plans for treating the patient?

Dr. Kranes: After the removal of the large nodes the temperature dropped considerably, although it did not become completely normal, and he was discharged home to return in a few weeks for nitrogen mustard therapy. We did not want to give it to him until he got over the effects of the operation.

Dr. Wyman: Why did you suggest nitrogen mustard rather than x-ray therapy?

Dr. Kranes: We did not know what to treat by x-ray therapy.

Dr. Wyman: You might treat the spleen and original tumor-bearing area.

Dr. Kranes: Dr. Welch found very few enlarged lymph nodes, and the original tumor was completely removed.

Dr. Welch: That is true; the only other palpable lymph nodes were near the large one.

Dr. Mallory: A bone-marrow biopsy was also done; it showed nothing of interest.

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ONE HUNDRED AND SEVENTIETH ANNUAL MEETING

The one hundred and seventieth annual meeting of the Massachusetts Medical Society, held at the Hotel Statler in Boston on May 22, 23 and 24, has become part of the record of this venerable organization. The attendance at the Society meeting was 2375 and that of the Auxiliary, held concurrently at the Hotel Bradford, was 197. The usual general sessions occupied much of the time. The annual meeting took place on the afternoon of Tuesday, May 22, on which occasion awards were presented, the President reported on the state of the Society and the annual oration was delivered by Dr. Donald Munro on the subject "How Specialized Is a Specialty?" The students from each of the medical schools of the state who had been recommended by their respective deans for the Society's annual prizes were Frank T. Bumpus of Tufts College Medical School, James B. Field of Harvard Medical School and Harry W. Fritts, Jr., of Boston University School of Medicine. Twelve fellows received pins commemorative of their fifty years of membership in the Society.

After the annual meeting the company adjourned to 22 Fenway for a reception at the new headquarters of the Society.

On the following morning the Shattuck Lecture, which was published in a recent issue of the *Journal*, was delivered by Sir Charles Harington, director of the National Institute for Medical Research, on the subject "The Role of the Basic Sciences in Medical Research."

Section meetings and luncheons were held on each of the three days of the meetings; the annual dinner took place on May 23, with Dr. Richard Ford, assistant professor of legal medicine at Harvard Medical School and medical examiner of Suffolk County, as guest speaker.

As usual, the Massachusetts Medico-Legal Society held its annual meeting during the sessions and the Massachusetts Physicians' Art Association presented its customary exhibition. As a special feature the Boston Medical Library also seized the occasion of the gathering of councilors to hold its own annual meeting prior to the meeting of the Council on May 21.

The annual meeting of the Woman's Auxiliary, which has now an enrollment of 1952 members, took place on May 22, with Mrs. Charles L. Shafer, national secretary, as guest speaker. The *Journal* takes pleasure in congratulating Mrs. William G. LeBrecht of Leominster on her accession to the presidency and Mrs. George E. McCabe of Worcester on her election to the position of president-elect. Mrs. Scott C. Applewhite, chairman of the national finance committee, was elected honorary member of the year.

The meeting of the Council held on the evening of May 21 was spirited, and a number of weighty problems were, if not solved, at least considered. The Committee on Public Relations, meeting jointly with the Committee on Education, had

recommended that the resolution introduced by the Norfolk District Medical Society concerning the requirements of the American Boards in regard to hospital residency programs be not approved; the Council referred this matter back to the committees for reappraisal.

The report of the Committee on Membership was amended to include as a policy of the committee the reduction of dues of full-time teachers and investigators in cases in which such payments might constitute a hardship, on the request of the dean or the administrative head of the institution where such a fellow or candidate for fellowship might be employed. This is an encouraging beginning in what should become a definite policy of the Society of making membership attractive to nonpracticing physicians.

A number of changes were made in the by-laws to bring these useful instruments up to date, and the formation of a Subcommittee on Alcoholism of the Committee on Rehabilitation and Chronic Disease was authorized.

The apparently arbitrary and dictatorial action of the administration of one of the smaller Boston hospitals in dismissing certain eminent members of its staff, who are fellows of the Massachusetts Medical Society, was brought out in the report of the Committee on Hospital and Professional Relations, affording an uninspiring example of the degree to which these relations can deteriorate. A basis on which such matters can be arbitrated will be the subject of intensive discussions with the Massachusetts Hospital Association in the near future.

In welcoming the new President, Dr. W. Richard Ohler, and the President-elect, Dr. Thomas H. Lanman, to their important posts, the *Journal* also takes the occasion to congratulate Dr. McKittrick for the able manner in which he has conducted the affairs of the Society during the year just passed.

PATHOGENICITY OF PENICILLIN-RESISTANT STAPHYLOCOCCI

THE increasing frequency with which penicillin-resistant staphylococci are being encountered has been the subject of many recent reports and has received editorial comment on frequent occasions in this and other journals. Sherris and Florey* have recently made a study of the relation of penicillin sensitivity in staphylococci to the clinical manifestations of infection by these organisms. Their results are of some interest, for they suggest that most of the penicillin-resistant strains that are being encountered may be much less significant than the sensitive ones in the pathogenesis of serious infections.

These workers tested 225 strains of staphylococci isolated from 224 lesions; 97 were found to be "sensitive" and 128 "resistant" by a ditch-plate method in which the ditch contained 10 units per ml. of penicillin incorporated into the agar. When tested for penicillinase production the resistant strains were found to produce the penicillin-inactivating enzyme, whereas the sensitive strains did not. In more quantitative tests the sensitive strains all fell within a limited range of sensitivity between 0.005 and 0.08 units per ml. by the method used; in other words, they were highly sensitive.

An analysis was also made of the types of lesions produced by the two kinds of staphylococci; this, too, indicated an important difference. Manifestations of inflammation were noted in 84 per cent of 57 lesions from which penicillin-sensitive staphylococci were isolated but in only 45 per cent of 78 lesions yielding penicillin-resistant strains. Suppuration was noted in 60 per cent of the penicillin-sensitive group as compared with only 27 per cent of the penicillin-resistant group. Signs of inflammation were absent in only 9 of the 57 lesions yielding sensitive staphylococci as compared with 43 of the 78 that yielded resistant strains, that is, 16 per cent as against 55 per cent. All these differences are statistically significant.

These findings are to some extent encouraging. They indicate that acute or closed and deep-seated infections are, in the main, still caused by penicillin-sensitive strains of staphylococci against which treatment with penicillin can be expected to yield favorable results. Signs of inflammation and suppuration were found significantly less often in lesions yielding resistant staphylococci. However, as

*Sherris, J. C., and Florey, M. D. Relation of penicillin sensitivity in staphylococci to clinical manifestations of infection. *Lancet* 1:309-312, 1951.

pointed out by the authors, this result cannot be interpreted as indicating that the resistant strains were less virulent. Furthermore, the sizable proportion of resistant strains that were associated with serious inflammatory and suppurative lesions indicates that the problem of the increasing occurrence of penicillin-resistant staphylococci is still of the greatest importance.

MAKING THE MOST OF MATURITY

THE average wife will outlive her husband not only because she is his junior but also because she is female. The kind of old lady she will be depends on her health. Neither of them should die too soon or live too long, and in the late fifties they should have a family health survey.

New and bigger taxes, increased cost of educating the children or assisting the newly married or helping with the cost of grandchildren (financial baby sitting) all cry out for a long-term cost-of-living plan. Further, if a couple should live too long, are they prepared to live together on a dwindling income? Are they psychologically preparing for retirement? What kind of old married couple do they want to be? Can these questions be answered by physicians? If not, how can they advise their patients?

Among the items in a recent issue of *Chronic Illness News Letter*, emanating from the Commission on Chronic Illness, is the announcement of Chicago University's "Making Most of Maturity" course. It is open only to persons aged fifty-five to sixty. Supported by a United States Public Health Service grant, it includes a complete medical examination, expert counseling on family adjustments, attitudes about employment and retirement, finances, philosophy of life for middle and later years, and even spiritual advice.

The need for orientation to the meaning of life is characteristic of post-adolescence and of middle life. Assessment of health is equally necessary at both times but is more often done in the earlier period — probably because health protection at the later period is still mostly a pious hope, for those who are fifty-five are on the ski-jump slope of the life-expectancy curve. Health protection as a personal service in middle and older years will become a reality only for those who have periodic examinations. In the meantime a course like the one in Chicago, offering instruction in financial, educational, psychological and spiritual planning, will soften blows that the years will bring. Such a course is commended to the Massachusetts Medical Society, to the State departments of health and adult education and to our specialists in the care of the aging.

HOME ON THE RANGE

THE scientific staff of the University of Wisconsin, according to the University News Service, has again demonstrated its extraordinary versatility in the matter of turning biologic know-how to account.

The most recent proposition has to do with the nation's natural lakes and waterways, which in times of emergency can be used as an accessory to pasture and rangeland for the production of food protein.

Wisconsin alone has over 6500 acres of small ponds and lakes, and these, properly prepared — like land — by the addition of lime, can be turned into pasturage for rainbow trout and bass.

Suitably cultivated pastureland of the orthodox variety can be made to produce annually from 100 to 200 pounds of carcass beef per acre; pasture ponds in the bog-lake country can be coaxed into the production of 50 to 75 pounds of fish to the acre, and eventually perhaps as much as the European carp ponds, with their annual harvests of over 150 pounds.

The thought, although not exciting, nevertheless carries with it a certain sense of security. As one meets the buffets of outrageous fortune in the problematical future there will be some comfort in the knowledge that something will be cooking, if only a trout, at home on the range.

Messrs. Lindsay & Blakiston, Philadelphia, have just published a new edition of Walker's celebrated work on "Intermarriage, or the mode in which, and the causes why, beauty, health and intellect result from certain unions; and deformity, disease and insanity from others." It is an exceedingly interesting book, and one that may profitably be read by adults.

Boston M. & S. J., *June 11, 1851*

MASSACHUSETTS MEDICAL SOCIETY

President's Message*

Before this meeting of the Council closes I should like to detain you for a few minutes while I outline certain personal views and ambitions concerning the immediate future of the Society.

I am assuming at the start that we will all subscribe to the following definition of the main purpose of the organization:

> To constantly improve the quality of medical practice in Massachusetts so that the people of this state may receive excellent medical care regardless of ability to pay.

This statement of principle is entirely in accord with the thoughts of our founders, 170 years ago.

This slogan, or motive, presents a challenge to all of us. How can we best meet this challenge?

In the first place, the Society is interested in and has given and will continue to give active, intelligent support to the work of the Blue Cross and Blue Shield, looking hopefully to the time when the coverage offered by these agencies will be much more extensive than at present and will contain no grounds for any serious controversy. Just how to cope with the difficulty of maintaining proper individual coverage during times of unemployment is uppermost in our thoughts. We are all hopeful that this problem will succumb to an early solution.

We are all interested, — and no one more so than myself, — in the improvement of both public and internal relations. Public relations is a matter best settled by the individual physician in his personal relations with patients. Recent editorial comment on this problem in the *New England Journal of Medicine*† makes excellent reading for all of us. In order to assist the physician in maintaining good public relations we have a Fee Committee and a Committee on Public Relations, both active in insuring to the public adequate constant medical coverage at a fee commensurate with ability to pay. In addition, we have a very active Director of Public Education and Information, much of whose work is directed toward maintaining good public relations. In the event that good public relations are not maintained and that the patient believes he has a grievance, we have and have had since 1871 a grievance committee, which we have called our Committee on Ethics and Discipline, to which such problems can be presented.

Internal relations is another problem, although also to some degree the concern of the Committee on Ethics and Discipline. It has long been my belief that given adequate facilities, practitioners could do much better work. I am interested therefore in the problem of improving medical facilities for the doctors in the districts apart from medical centers. I believe that this can best be done by using the local or community hospitals as a source of improved facilities. But this is of no help if the local physician is not affiliated with a good hospital. Consequently, it is my firm belief that one of the most important things to labor for is that every member of the Massachusetts Medical Society may have both the privilege of sending his patients to a good local hospital and the privilege of turning to this hospital for the solution of laboratory problems.

It goes without saying that in order to constantly improve medical care in this state or any state continuous medical education is necessary. In this state, postgraduate instruction has been free of charge and has been open to all physicians, whether members of the Massachusetts Medical Society or not. We hope in the near future so to enlarge the scope of graduate training as to include the medical schools and well-established clinics in a united effort centering in this Society. If this plan is effective then we may all look forward to the organization of an institute of postgraduate medical instruction in this state.

There are still to be solved the many problems that arise in relation to hospital practices, especially as applied to certain medical specialties. Under the stimulus of your retiring President, we have just started a move that gives hope of solving this problem and of setting up in this state a pattern that we all can follow.

If we can, in the next year or so, solve in this state the problem mentioned above; if we can set up a postgraduate program that will satisfy the needs of our own members and that may attract students from areas far and wide; if we can improve medical facilities — tools of the trade — for all members by assuring them of a place in a good hospital; if we can make it clear to all physicians that good public relations begin with the physician himself; if we can assure adequate coverage to all citizens at all times; and if we can acquaint both people and physicians with the fact that there is a proper committee to which they can come with their grievances; if we can work out a satisfactory guide for the conduct of certain hospital practices — if we can do

*Delivered by the incoming President at the meeting of the Council, May 21, 1951.

†Editorial. Relations, public and private. *New Eng. J. Med.* 244:342, 1951.

these things, then, in my opinion we have no need to worry about socialized, federalized or any other type of medicine. The troubles that confront us are of our own making; only we, acting together in a truly co-operative spirit, can solve these problems to the end that good medical practice for all people may prevail.

With such a thought in mind, and believing most heartily in the good sense and public spirit of this Society, I look forward to the coming year with much hope and expectation. I believe we can have a good year together and that the people of the state will benefit thereby.

W. Richard Ohler, M.D.

DEATHS

Cleaves — Ezra E. Cleaves, M.D., of Rockport, died on January 9. He was in his seventy-seventh year.

Dr. Cleaves received his degree from Harvard Medical School in 1900. He was a past president of the Essex South District Medical Society. For many years he was secretary of the medical staff of the Addison Gilbert Hospital in Gloucester.

A son and three grandchildren survive.

Hogan — Joseph A. Hogan, M.D., of Lawrence, died on December 13. He was in his seventy-ninth year.

Dr. Hogan received his degree from Harvard Medical School in 1897.

Two sisters survive.

Levenson — Walter S. Levenson, M.D., of Chestnut Hill, died on September 22. He was in his fifty-fourth year.

Dr. Levenson received his degree from Harvard Medical School in 1922. He was a member of the American College of Surgeons and the New England Pediatric Society and a fellow of the American Medical Association.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

COMMUNICABLE DISEASES IN MASSACHUSETTS FOR APRIL, 1951

Résumé

Disease	April 1951	April 1950	Seven-Year Median
Chancroid	7	0	2
Chicken pox	1654	1615	1973
Diphtheria	7	17	18
Dog bite	1395	1160	1161
Dysentery, bacillary	4	7	7
German measles	264	258	381
Gonorrhea	130	184	319
Granuloma inguinale	0	0	0
Lymphogranuloma venereum	0	1	1
Malaria	1	0	4
Measles	1996	2022	3491
Meningitis, meningococcal	5	6	6
Meningitis, Pfeiffer-bacillus	3	2	3
Meningitis, pneumococcal	1	8	7
Meningitis, staphylococcal	0	0	0
Meningitis, streptococcal	0	0	1
Meningitis, undetermined	4	3	4
Mumps	1612	899	1346
Poliomyelitis	0	0	1
Salmonellosis	1	7	6
Scarlet fever	580	624	812
Syphilis	94	125	303
Tuberculosis, pulmonary	234	159	225
Tuberculosis, other forms	18	7	12
Typhoid fever	1	1	3
Undulant fever	1	3	3
Whooping cough	172	544	476

Comment

The only disease notably above the seven-year median for April is mumps.

Diseases with prevalence below the seven-year median for the month are chicken pox, diphtheria, bacillary dysentery, German measles, measles, poliomyelitis, salmonellosis, scarlet fever, typhoid fever, undulant fever and whooping cough.

The prevalence of mumps is the highest reported in April for three years, and for the seventh consecutive month the number of cases reported is higher than in the corresponding month of the previous year.

The seven cases of diphtheria are the fewest ever reported for April.

The single case of undulant fever is the lowest figure for this disease in April since 1934.

The 172 cases of whooping cough are the fewest ever reported in April.

For the first month since last May, no cases of poliomyelitis were reported.

Geographical Distribution of Certain Diseases

Anthrax was reported from: Haverhill, 1; Merrimac, 1; total, 2.

Diphtheria was reported from: Boston, 1; Cambridge, 1; Danvers, 1; Dedham, 2; Halifax, 1; New Bedford, 1; total, 7.

Dysentery, amebic, was reported from: Murphy Army Hospital, 1; total, 1.

Dysentery, bacillary, was reported from: Springfield, 1; Worcester, 3; total, 4.

Encephalitis, infectious, was reported from: Fall River, 1; Lynn, 1; Waltham, 1; Watertown, 2; total, 5.

Hepatitis, infectious, was reported from: Grafton, 1; Medford, 1; Murphy Army Hospital, 5; Norwood, 1; Worcester, 1; Wrentham, 1; total, 10.

Lymphocytic choriomeningitis was reported from: Watertown, 1; total, 1.

Malaria was reported from Murphy Army Hospital, 1; total, 1.

Meningitis, meningococcal, was reported from: Braintree, 1; Chelsea, 1; Holyoke, 1; Springfield, 1; Wilmington, 1; total, 5.

Meningitis, Pfeiffer-bacillus, was reported from: Andover, 1; North Attleboro, 1; Williamsburg, 1; total, 3.

Meningitis, mumps, was reported from: Stoughton, 1; total, 1.

Meningitis, pneumococcal, was reported from: Middleboro, 1; total, 1.

Meningitis, undetermined, was reported from: Bedford, 1; Fort Devens, 2; Sheffield, 1; total, 4.

Salmonellosis was reported from: Leicester, 1; total, 1.

Septic sore throat was reported from: Adams, 5; Boston, 8; Milton, 1; Westford, 1; Worcester, 1; total, 16.

Tetanus was reported from: Bridgewater, 1; total, 1.

Trichinosis was reported from: Boston, 1; Brockton, 1; Waltham, 1; total, 3.

Typhoid fever was reported from: Agawam, 1; total, 1.

Undulant fever was reported from: Brockton, 1; total, 1.

CORRESPONDENCE

SUSPENSION OF LICENSE

To the Editor: At a meeting of the Board of Registration in Medicine held May 18, it was voted to suspend the registration of Dr. Louis B. Silverstein, 756 Moody Street, Waltham, for three months.

Robert C. Cochrane, M.D., *Secretary*
Board of Registration in Medicine

State House
Boston

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Short Textbook of Radiotherapy for Technicians and Students: With a supplementary chapter for the dermatologist. By J. Walter, M.A., B.M. (Oxon.), M.R.C.P. (Lond.), D.M.R.E. (Camb.), consultant radiotherapist and deputy medical director, Sheffield National Centre for Radiotherapy; and H.

Miller, M.A., Ph.D. (Camb.), F. Inst. P., physicist, Sheffield National Centre for Radiotherapy. With a foreword by J. L. A. Grout, M.C., F.R.C.S. (Ed.), F.F.R., D.M.R.E., vice-president, Faculty of Radiologists. 8°, cloth, 444 pp., with 199 illustrations. Philadelphia: Blakiston Company, 1950. $6.00.

The text of this new book is based on a course of lectures given originally to student radiographers. The early chapters are devoted to the physics of the x-ray and radioactive materials. These are followed by chapters on the biologic effects of radiation, the methods of radiation by radium and the x-ray, the principles of treatment and dosage, technic in malignant and nonmalignant cases, protection, duties and responsibilities and radiotherapy in dermatology. The appendix gives the recommendations of the British X-Ray and Radium Protection Committee. There is a supplementary chapter on artificial radioactivity and its medical applications. The material is well arranged and well written. The printing was done in Great Britain, and the publishing is excellent.

Vocational Rehabilitation of Psychiatric Patients. By Thomas A. C. Rennie, M.D., Cornell University Medical College and the New York Hospital; Temple Burling, M.D.; and Luther E. Woodward, Ph.D., Division on Rehabilitation, National Committee for Mental Hygiene. 8°, cloth, 133 pp. New York: Commonwealth Fund, 1950. 75c.

This study was limited to paroled or discharged hospital patients and largely to post-psychotic persons, of whom 77 per cent were satisfactorily employed at the time the case was closed by the rehabilitation bureau. The authors stress the need for a conclusive statistical evaluation of vocational-rehabilitation efforts with the psychiatrically handicapped, and the need for more adequate information by counselors about the emotional satisfactions people need to find in their jobs.

Adrenal Cortex: Transactions of the First Conference, November 21-22, 1949. Edited by Elaine P. Ralli, New York University College of Medicine. 8°, cloth, 189 pp., with 21 illustrations and 7 tables. New York: Josiah Macy, Jr., Foundation, 1950. $2.00.

The papers presented at this first conference comprised the relation of chemical structure of adrenocortical hormones to biologic activity, regulation of adrenocortical secretion, clinical studies with cortisone and ACTH, steroid metabolism in the adrenal cortex and relation of vitamins to adrenocortical function. Sixteen persons took part in the conference and discussed the various papers.

Your Hair: Its health, beauty and growth. By Herman Goodman, M.D. 8°, cloth, 287 pp., with illustrations. New York: Emerson Books, Incorporated, 1950. $2.95.

This popular book discusses in simple language the anatomy, physiology and hygiene of the hair, and diseases of the scalp. There are special chapters on baldness, superfluous hair, curling and waving and also on the relations of vitamins and diet to healthy hair, and hair problems in childhood.

Klinische Psychopathologie. By Kurt Schneider, professor, University of Heidelberg. Third edition. 8°, cloth, 179 pp. Stuttgart: Georg Thieme, 1950. Ganzleinen DM 11.40/ $2.70. (Distributed by Grune and Stratton, New York.)

In this third edition a small book on clinical psychopathology has been revised and expanded by the addition of chapters on psychopathic personalities and the psychoses of imbecility. A bibliography of references to the modern literature pertaining to the subject is appended to the text. The book should be in all collections on the subject.

Nursing in Prevention and Control of Tuberculosis. By H. W. Hetherington, M.D., M.R.C.P. (London), chief of clinic, Henry Phipps Institute of the University of Pennsylvania, and assistant professor of medicine, University of Pennsylvania School of Medicine; and Fannie W. Eshleman, R.N., S.B., supervisor of public-health nursing, Henry Phipps Institute of the University of Pennsylvania, and lecturer on tuberculosis nursing, Department of Nursing Education, University of Pennsylvania. Third edition. 8°, cloth, 361 pp., with illustrations. New York: G. P. Putnam's Sons, 1950. $4.50.

This standard textbook, first published in 1941, has been revised and brought up to date. The book is written for nurses and other persons who have to care for tuberculous patients. It is well published and should prove useful.

Modern Trends in Orthopaedics. Edited by Sir Harry Platt, M.D., M.S., F.R.C.S., professor of orthopedic surgery, University of Manchester, consultant adviser in orthopedics to the Ministry of Health, and president, Société Internationale de Chirurgie Orthopédique et de Traumatologie. 8°, cloth, 497 pp., with 222 illustrations. New York: Paul B. Hoeber, Incorporated, 1950. $10.00.

This is a composite work consisting of 14 chapters on special subjects written by authorities in their particular fields. Each chapter is documented with a bibliography of references to recent literature.

The printing was done in Great Britain, and the publishing is excellent. The book is recommended for all medical libraries and to all physicians and surgeons interested in orthopedics.

NOTICES

ADDRESS ON MULTIPLE SCLEROSIS

Dr. Tracy Putnam will address the Neurobiologic Unit of the Boston State Hospital Research Department and the Massachusetts Chapter of the National Multiple Sclerosis Society at the auditorium of the Boston State Hospital on Thursday, June 14, at 11 a.m. Dr. Putnam will speak on "New Advances in Multiple Sclerosis."

ARTHRITIS AND RHEUMATISM FOUNDATION FELLOWSHIPS

The Arthritis and Rheumatism Foundation is offering research fellowships in the basic sciences related to arthritis. Fellowships will be granted at both the predoctoral and postdoctoral levels. The predoctoral fellowships will range between $1500 and $3000 per year, the postdoctoral from $3000 to $6000. The deadline for these applications is November 15, 1951. Application forms may be obtained by writing the Medical Director, Arthritis and Rheumatism Foundation, 535 Fifth Avenue, New York 17, N. Y.

SOCIETY MEETINGS AND CONFERENCES

JUNE 9 AND 10. American Society for the Study of Sterility. Page 274, issue of February 15.

JUNE 11-15. American Medical Association. Annual Session. Atlantic City, New Jersey.

JUNE 11-15. Physicians' Art Exhibit at A.M.A. Meeting. Page 614, issue of April 19.

JUNE 14. Address on Multiple Sclerosis. Notice above.

JUNE 15-17. American Electroencephalographic Society. Page 346, issue of March 1.

JUNE 18-20. American Neurological Association. Page 614, issue of April 19.

JUNE 20-23. American Orthopaedic Association. Page 422, issue of March 15.

JUNE 24-28. American Society of Medical Technologists. Page 858, issue of May 31.

SEPTEMBER 4-8. American Congress of Physical Medicine. Page 238, issue of February 8.

SEPTEMBER 12-14. Biological Photographic Association, Inc. Annual Meeting, Boston.

SEPTEMBER 19. American Medical Writers' Association. Page 1066, issue of December 28.

SEPTEMBER 19-21. Mississippi Valley Medical Society. Page 1066, issue of December 28.

SEPTEMBER 30-OCTOBER 2. New Hampshire Medical Society. Annual Meeting. Equinox House, Manchester, Vermont.

OCTOBER 31. New England Obstetrical and Gynecological Society. Hotel Somerset, Boston.

NOVEMBER 7-19. Pan-Pacific Surgical Association. Page 820, issue of May 24.

JULY 8-11, 1952. Thirteenth British Congress of Obstetrics and Gynaecology. Page xv, issue of December 14.

(*Notices concluded on page xiii*)